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Original Contributions

THE AURICULAR WAVE

AN EXHAUSTIVE INQUIRY INTO THE PHYSIOLOGICAL AND PATHOLOGICAL VARIATIONS OF THE P WAVE (OR AURICULAR WAVE) OF THE ELECTROCARDIOGRAM

by

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Introductory Note—The subject of Electrocardiography, has not unfortunately, been received kindly by the medical profession of this country. In spite of its growing importance and usefulness in the diagnosis and assessment of prognosis of cardio-vascular disorders, it is a matter of regret to note that until as late as 1940, this country could not boast of one single large-scale investigation into the subject of electrocardiography. The electrocardiographic standards so far adopted in India, have been based on insufficient numbers or small series of European or American subjects and hence are inadequate for our needs, they are not in keeping with the growing interest of the clinician in the subject of electrocardiography.

The present work represents an elaboration and continuation of work done by one of us (R J V) in 1939 and 1940 on the subject of electrocardiographic standards, with the aid of a medical research grant from the Trust of the late Sir Ratan Tata. Part of these electrocardiographic studies have appeared in print in recent issues of the "Proceedings of the Indian Academy of Sciences" and require no elaboration.

The present work, though it owes its inspiration to and depends for part of its data on the published work of 1940, is, nevertheless a distinct contribution to the subject of electrocardiography, in as much as it deals with one single deflection of the electrocardiogram (viz the P wave) in a much more exhaustive fashion and also brings into consideration and study, a new and more elaborate aspect of the subject, viz the behaviour of the P wave under conditions of ill-health or disease. The normal or physiological P wave gives birth to its pathological counterpart, viz, the P wave of disease.

The correct interpretation of any electrocardiogram demands, first and foremost, a thorough knowledge of the normal state, with all its physiological limits and vagaries. To deal with "the P wave pathological" without a fair knowledge of its normal variations and behaviour is like treating a diseased body with no knowledge of basic anatomy or physiology. In either case, the results are likely to prove disastrous.

Selection of Material—Subjects for the present electrocardiographic investigation were selected from diverse sources. Besides "normal" electrocardiograms of well over a hundred school-boys of the Bharda New High School, of over fifty girls from the Parsee Girls' High School, and of numerous friends, relatives and students, the electrocardiograms of numerous patients, both hospitalized and private, have been collectively responsible for furnishing the necessary sub-stratum or data for this paper.

The P Wave Its Causation and Nature—The P wave or deflection represents the early electrical activity of the auricular musculature hence the application of the designation "auricular wave" to the deflection. The P wave has been defined by Katz as "the time register of the spread of the excitation process through the auricles" and by Frank Wilson as "the graph of the electrical effects produced by the spread of the excitatory process over the auricular muscle".

It has been experimentally demonstrated by various observers (Samoiloff, 1909, Kraus and Nicolai, 1910, Lewis, Meakins and White, 1914, Eyster and Meek, 1913) that the P wave is nothing more or less than a composite representation of the excitation wave spreading over the auricular muscle from the S A node. It reflects the physiological activity of the muscle-fibres of the auricles. Contraction of the muscle fibres, wherever induced, creates a negative electrical potential, which can be registered by the use of the galvanometer.

Due to the gradual and progressive spread of the excitation wave over the heart-muscle, fibres which receive the stimulus first naturally start contracting first. Muscle-activity, as shown by electrocardiographic deflection, therefore, precedes the rise of pressure within the auricles. Accordingly, the electrical deflection or P wave caused by auricular muscle activity commences just prior to the rise of intra-auricular pressure caused by auricular systole. Also, the P wave ends some time before the actual completion of auricular systole according to Pardee, from point of time, "the end of P coincides with the top of the rise of intra-auricular pressure".

There has been considerable controversy in medical circles as to whether electrical deflections like P and Q-R-S are due to a process of "excitation" or "contraction". According to Pardee, such a distinction is unwarranted and unnecessary.

It is interesting to enquire into the reason why the ventricular deflection (Q-R-S and T) of the heart is so much more complex than

the auricular deflection (P wave) The difference depends on the different modes of spread of the excitation wave in the auricular and ventricular chambers of the heart In the case of the auricle, the stimulus or wave spreads out radially from a large S. A. node into a fairly small bulk of auricular musculature, in the case of the ventricles, on the other hand, the contraction stimulus has to take a very devious route through the Bundle of His, through its branches and through the terminal ramifications of Purkinje

The Complete Auricular Wave—The real auricular wave or deflection does not merely consist of a P wave, actually, the positive deflection of P is followed by a "dip" or depression, the so-called "auricular T-wave" or the "Ta wave" The existence of this negative Ta wave (or downward deflection of the P-R segment) was observed many years ago by numerous observers, but its true relationship to auricular systole was first noted in 1924 by Einthoven The Ta wave is usually negative or below the iso-electric line, in a direction opposite to that of the P wave, the deflection below the zero-level may even be as great as 2.5 mm In a series of 200 normal adults, the average value of the deflection for all leads was 0.31 mm Average values for the individual leads were 0.28 mm for Lead I, 0.36 mm for Lead II and 0.30 mm for Lead III In other words, the deflection is usually maximal in Lead II The average values of P-R level were not markedly different in the two sexes, although slightly higher values were encountered in males

The Ta deflection begins from the end of P and comes to an end during the rise of the ventricular T wave Its frequent occurrence in electrocardiographic records was brought to light by the researches of Sprague and White (1925) In records with unduly large P waves the P-R level is often deflected to a greater degree than in normal records There appears to be a rough direct relationship between the size of the P waves and the degree of deflection and length of the auricular T wave From a study of normal records, it appears that the deflection of P-R is much more directly related to the amplitude of P than to its duration, as a matter of fact, the deflection of P-R appears to be independent of the duration of P

According to Katz (1941), the complete auricular wave is much more complex than is usually believed, it is in fact, very much like a miniature ventricular complex There is a large initial, usually upright, P wave or auricular complex followed by a short intermediary segment (which may be non-existent) and a terminal shallow deflection of long duration (Ta wave), practically always in a direction opposite to that of the initial P deflection

A detailed study of the "complete auricular wave" is rendered possible in cases of auriculo-ventricular block by the absence of the ventricular deflections

Form of the P Wave—It is customary for text-books to describe the P wave as a "smooth and rounded elevation", such a description

has been copied from book to book, without a proper enquiry into the exact state of affairs. It has been demonstrated by me (R.J.V.) in previous communications, that the pointed form of P wave is more commonly encountered than the "rounded form", both in school children and grown-ups.

TABLE I.—Percentage Incidence of the 'Pointed' or 'Rounded' Form of P wave

	No. of records studied	Percentage Incidence		Miscellaneous forms
		Pointed form	Rounded form	
1 School boys	100	75	70	31
2 School girls	50	33	17	10
3 Normal adults 2nd to 5th decades (inclusive)	200	10	17	17

Besides "pointed" and "rounded" forms, the P wave displays a variety of other forms, the most important being the 'bifid form', the flat or iso-electric form, the inverted or negative form and the diphasic form.

TABLE II.—Percentage Frequencies of the Different Forms of P wave

Description of P wave	School boys			Girls			Adults		
	I	II	III	I	II	III	I	II	III
1 Flat or isoelectric	4	1	15	0	0	10	2.5	2	6.5
2 Bifid	0	0	5	0	0	0	1.5	2.5	2
3 Inverted or negative	2	0	14	0	0	4	0	1.0	12.5
4 Diphasic	2	4	10	2	0	22	1.5	1.0	0.5

It will be observed that the incidence of all abnormal forms of P, with the exception of bifid form is highest in Lead III. As a matter of fact, the majority of authors regard inverted or diphasic P waves in Lead III should be considered abnormal if the waves in question are unduly "large" or "broad".

A Further Study of the Diphasic form of P in Normal Records—There are two main forms of diphasic P waves discernible. In Type I, the primary deflection is upward followed by a downward deflection. This is much the commoner type in normal records. In Type II, the initial deflection is downward while the final deflection is upward, according to Ashman and Hull. Type I is encountered in Lead III in about 5 per cent of normal electrocardiographic records while type II is rarely encountered in normal hearts. In my (R.J.V.) series of 350 normal records, the incidence rate of Type I was about 4.5 times as high as that of Type II. One can therefore truthfully state that when the P wave is diphasic in normal records, the initial deflection is usually upward. A point of some importance with regard to Type I diphasic P wave has been raised recently by Ashman and Hull. The initial upward deflection of Type I may be low enough to be missed.

in which case the P wave is likely to be erroneously labelled "an inverted P wave"

The tendency for the P wave to vary in form from cycle to cycle or from time to time in perfectly healthy individuals is difficult to explain, inconstancy or variability of form of the P wave is perhaps due to an inconstancy or variability in the path pursued by the excitation wave in the substance of the auricular muscle. It may also be dependant to some extent on the phases of respiration

With regard to the form of P wave, the presence of a quick upstroke with a very slow down-stroke or vice versa should be regarded with suspicion, according to Ashman and Hull, such changes are more common in the presence of heart disease than in its absence

Notching of P Waves—"Notching of P" was once regarded as a reliable sign of auricular hypertrophy. The validity of this statement has been questioned from time to time. Various observers have independently described notching of the P wave in a fair percentage of perfectly normal records. Thus Lewis and Gilder (1912) out of their series of 52 normal records, found 17 records with notching in one or more standard leads, P1 was notched in 2 records, P2 in 17 and P3 in 10. In the series of 200 normal records, reported by Shipley and Hallaran (1936), notching of P was noted in 30 per cent. Ashman and Hull report notching of P in one or more leads in 32 per cent of normal records. In the three series of normal records studied by me (R J V) notching of P was observed quite frequently. Notching of P in one or more leads was observed in 35 per cent of records from schoolboys, in 44 per cent of records from school girls and in 38.5 per cent of records from adults. In other words, over one-third of normal records display notching of P waves. Ashman and Hull (1941) found the incidence of P wave notching lower in children than in adults, In my series (R J V), there was little or no difference in incidence between the two age-groups (39.5 per cent for children and 38.5 per cent for adults). The normal notch, as mentioned by Ashman and Hull, occurs more frequently on the upstroke of P than on the down-stroke, we find the notch about $1\frac{1}{2}$ times as often on the upstroke as on the downstroke

TABLE III.—P wave notching in the three leads
(Percentage Frequencies)

	School boys	School girls	Adults
Lead I	14	14	18.5
Lead II	25	30	41.5
Lead III	18	14	20.5

Out of a series of 350 normal records, comprising of all age periods, there were only 6 records with notching of P in all the three leads of the record (Incidence of 1.7 per cent)

Notching of the normal P is said to occur most frequently in Lead II. Table III gives an idea of the incidence of P wave notching in different leads at various periods of life

It will be observed that notching is encountered most frequently in Lead II and least of all in Lead I

The significance of Notching P—The mechanism of notching of the P wave has been well explained by Pardee (1933), in his opinion, the normal P wave represents a synchronous overlapping of two electrical effects, one from each auricle, if for some reason, the path of the excitation wave becomes tortuous or altered in one auricle, then the two electrical effects are not superimposed one on top of the other, and notching results

The time is past when notching of P was regarded in medical circles as a reliable and constant sign of auricular hypertrophy or disease. Today, the profession has come to realize that notching of P "must be accepted as one of the normal variations of the P wave" (Pardee). This is obvious from the high incidence of such P waves reported in various series of normal records.

There are, however, three special types of P wave notching, which we feel cannot be included in the category of "normal variations"

(1) It has been shown by Hoskin, Jonescu (1940), Shipley, Hal-laran (1936) and others that the association of "notching" with "a large amplitude" in the P wave cannot be regarded as a normal variation. Such a combination is said to be very suggestive of mitral stenosis. In a series of 350 normal records (1940), from diverse age-groups, there were only 10 records (i.e. incidence of 2.9 per cent) with large and notched P waves, P waves over 2 mm in amplitude were considered as "large". There was no evidence of a valvular lesion in any of these 10 cases. Nevertheless, the association of P wave notching with a large amplitude occurs with sufficient rarity to prevent us from including this phenomenon in the category of normal variations.

(2) Notching associated with increase in width or duration of P should be regarded with suspicion, as such a combination is suggestive of disease.

(3) Deep notching or multiple notching of P is much more significant of disease than mere notching of the P wave.

Height or Amplitude of the P Wave—In the opinion of Pardee (1933) the height of the normal P wave should lie between 1 and 2 mm in the lead of maximum excursion, in the event of P in one lead being isoelectric or diphasic, the amplitudes in the other two leads being about equal, the value of P should be between 0.9 and 1.8 mm.

After a study of electrocardiograms from 52 normal subjects, Lewis and Gilder (1912) gave the average value of P in Lead I as 0.52 mm in Lead II as 1.16 mm and in Lead III as 0.81 mm. Ashman and Hull's (1941) corresponding figures are 0.55, 1.36 and 0.83. Hoskin and Jonescu (1940), after a study of 50 cardiograms from normal lady students, gave the average value of P as 1.74 mm (range being 0.5 to 5.0 mm). In a combined series of 350 normal subjects (1940) the average value for P, taking the three standard leads into consideration, was 1.05 mm for males and 0.94 mm for females (range for males being—2.0 to 3.1 mm and for females—1.3 to 3.2 mm). The

average value of P was consistently higher in males than in females in all the age-groups studied (see Table IV) This is in conformity with the finding of Shipley and Hallaran (1936) who gave the average value of P in Lead II as 1.41 mm for males and 1.30 mm for females

In my series (RJV) the highest values for P wave amplitude were observed in Lead II, as has been shown previously by various authors

In adults the average values for P wave were somewhat higher in the 4th and 5th decades than in the other decades of life (Table IV)

TABLE IV—An Analysis of the Amplitude of the P Wave
(Values in mms)

Decade	Value	MALES			FEMALES		
		Lead I	II	III	I	II	III
2nd	Average	0.85	1.12	0.72	0.80	1.26	0.62
	Minimum	—0.3	0.0	—1.1	0.0	0.0	—1.0
	Maximum	2.1	3.0	3.0	1.8	2.2	3.2
3rd	Average	0.91	1.51	0.84	0.84	1.22	0.55
	Minimum	0.0	—0.2	—2.0	0.0	0.0	—1.3
	Maximum	2.0	3.1	2.0	1.6	2.3	3.0
4th	Average	0.86	1.02	0.08	0.79	1.10	1.00
	Minimum	0.0	0.0	—0.5	0.0	0.0	—0.2
	Maximum	2.3	3.1	2.0	1.8	2.0	2.1
5th	Average	1.00	1.20	0.90	0.90	1.42	0.82
	Minimum	0.0	0.0	—1.2	0.0	—0.2	—1.0
	Maximum	2.1	2.3	2.2	1.6	2.2	1.8
For all decades	Average	0.95	1.44	0.77	0.83	1.25	0.74
	Minimum	—0.8	—0.2	—2.0	0.0	—0.2	—1.3
	Maximum	2.3	3.1	3.0	1.8	2.3	3.2

TABLE V—An Analysis of the P Wave Duration
(Values in seconds)

Decade	Value	MALES			FEMALES		
		Lead I	II	III	I	II	III
2nd	Average	0.078	0.092	0.071	0.070	0.090	0.071
	Minimum	0.04	0.04	0.04	0.04	0.03	0.03
	Maximum	0.15	0.14	0.13	0.14	0.14	0.12
3rd	Average	0.083	0.098	0.074	0.080	0.094	0.073
	Minimum	0.06	0.05	0.03	0.04	0.06	0.04
	Maximum	0.15	0.16	0.14	0.14	0.11	0.10
4th	Average	0.070	0.090	0.084	0.078	0.090	0.081
	Minimum	0.04	0.04	0.04	0.04	0.03	0.06
	Maximum	0.12	0.14	0.14	0.14	0.15	0.12
5th	Average	0.080	0.088	0.082	0.078	0.084	0.070
	Minimum	0.04	0.04	0.06	0.04	0.06	0.04
	Maximum	0.14	0.15	0.14	0.14	0.13	0.14
For all decades	Average	0.080	0.094	0.078	0.070	0.090	0.076
	Minimum	0.04	0.04	0.03	0.04	0.03	0.03
	Maximum	0.15	0.15	0.14	0.14	0.15	0.14

The amplitude of P may vary from cycle to cycle in many perfectly normal records, hence the difficulty in determining the correct amplitude of P in any given record. The variability in amplitude of P is ascribed by Ashman and Hull (1941), to "fluctuations in the

tonic activity of the efferent cardiac innervations" Larger variations in amplitude, as are witnessed in the case of sinus arrhythmia, may be due to a "phasic shift" in the position of the S A pacemaker

Duration or Width of the P Wave (See Table V) —The duration of P is measured in seconds from the beginning to the end of the P wave The most useful and practical measurement of P wave duration is in the lead of maximum width, which is frequently in Lead II If an impulse happens to travel perpendicularly or at right angles to the line of the lead, at the commencement or termination of the inscription of the P wave, then part of the P wave will go unrecorded on the electrocardiogram and the wave will appear to be of shorter duration in that lead than is actually the case This is the explanation forwarded by Ashman and Hull (1941) to explain the difference in duration of P in Leads I and II

The average duration of the P wave is given as 0.09 second by Shipley and Hallaran, (1936) 0.076 second, by Hoskin and Jonescu (1940) and just over 0.08 sec by Ashman and Hull (1941) In my series of 350 normals, (R J V 1940), the average duration of P was 0.084 sec for males and 0.082 sec for females The average duration was higher in males by 0.002 sec These findings are in accordance with those of Hoskin and Jonescu and of Ashman and Hull who report slightly higher figures for P wave duration in males than females From a detailed study of P wave duration, it appears that the average value of P duration shows little or no alteration with age (see Table V) The highest value encountered amongst normals for P wave duration in my series (R J V) was 0.14 sec, this being encountered 7 times in a series of 350 records (incidence of 2 per cent) The usually accepted higher limit for P wave duration is 0.10 sec, in Ashman and Hull's series, this value was exceeded only once while in Shipley and Hallaran's series it was exceeded three times

In my series (R J V), the average values of P wave duration for the three individual leads were as follows Lead I—0.0795, Lead II—0.090 sec, Lead III—0.072 sec for children and Lead I—0.080, Lead II—0.092, Lead III—0.077 for adults It will be obvious from these figures that the highest values for P wave duration are encountered in Lead II and the lowest in Lead III An increase in the duration of P denotes an increase in the time taken by the impulse to invade or spread through the whole of the auricular musculature Increase in bulk of the latter will therefore cause a corresponding increase in the duration of P

Such an increase in duration of P may arise from increased bulk of the auricular musculature or from diminution in the velocity of impulse spread or both

Physiological Alterations in the P Wave—Influence of Age—In the opinion of many authors the P wave in infancy and childhood is "shorter in duration" and "considerably taller" than in adults The P wave of infancy has been described as "peaked" Not having studied

the P waves of infancy, we are not in a position to confirm or refute the validity of the above contention in its entirety. A study of the normal P wave of 150 children and 200 adults has however disclosed the following averages for the height and diameter of the P waves

TABLE VI—P Wave Values in Children and Adults

	Children		Adults		Comment
	Male	Female	Male	Female	
P amplitude	0.80	0.88	1.05	0.94	amplitude increased
P duration	0.08	0.08	0.084	0.082	duration increased

From Table VI, it appears that the P wave of childhood may be actually slightly smaller in size and shorter in duration than the P wave of adults. The same cannot be said, however for the P wave of infancy, as the latter wave has not been included in the present study.

Influence of Habitus or Constitution—In the hypersthenic or broad type of chest, the P & T waves are both small in Lead III and may even be inverted. In the case of persons with a slender build or of the hyposthenic type, the lowest P wave is usually witnessed in Lead I. This has been attributed by Ashman and Hull (1941) to the downward and leftward direction taken by the impulse after leaving the S A Node.

Position of the Diaphragm—A low diaphragm as in cases of asthma or in individuals with "long narrow chests" is usually associated with low voltage P waves in Lead I. In the case of a high diaphragm low P waves are encountered in Lead III.

Effects of respiratory movements—Respiratory movements are certainly capable of modifying or altering the various deflections of the electrocardiogram. The effects are most evident in the Q-R-S complex and least evident in the P waves. This is explained by the fact that the base of the heart (comprising mainly of the auricles) is relatively much more fixed by the attachment of the vascular pedicle than the much more freely mobile apex, also the auricles being further away from the diaphragm than the ventricles, are less likely to be effected by respiratory excursions of the diaphragm. It has been shown by Einthoven and his collaborators (1913), with the use of the equilateral triangle method, that variations in amplitude of P with respiration are due to 2 main factors viz (1) Rotation of the heart around a dorso-ventral axis and (2) Fluctuations in the tone of the vagus nerve.

Lewis, Meakins and White (1914) have also called attention to the influence of respiratory movements, the "lie of the heart" and other factors on the size and form of the P wave.

Influence of Fear in P Waves—In 1930 it was observed by Bier that mental excitement of a pleasant type frequently increases the amplitudes of the P, R and T waves of the electrocardiogram. More recently, Mainzer and Krause (1940) have investigated the influence of fear on the Electrocardiogram. The emotional stimulus used was "fear prior to operative anaesthesia". In 7 out of 53 cases the P and T waves were observed to become high and sharply pointed, as in cases of neuro-circulatory asthenia.

Influence of Extrinsic Cardiac Nerves on the P Waves—Einthoven, in 1908 showed that section of the vagus in dogs causes a marked increase in the size of the P wave. This was confirmed by Rothberger and Winterburg in 1910, who also demonstrated a diminution of P waves after section of the cardiac accelerator nerves.

(to be continued)

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CARCINOMA OF THE LARYNX*

by

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Cancer of larynx, which would be 100 per cent fatal, if left to itself, gives 80 to 85 per cent cures if the public and the general practitioner were to realise what a continued change in voice or a continued discomfort in the throat in an adult could mean. Even in some of the neglected cases of Intrinsic cancer, cure is as high as 45 per cent while in the other type of hopelessly advanced Extrinsic cases, we have obtained comparatively gratifying results and it is this later type which comprises unfortunately a large majority of the cases in our country and particularly more so in our K E M Hospital type of practice.

Although irradiation plays a very great part both in the curative and palliative treatment of cancer and it is the method of choice in extrinsic Cancer larynx, grade III and IV, and has, in many cases, to supplement surgical procedures, yet we cannot say much about it, because on account of circumstances beyond our hospital control, it was not available, to us, during the period under consideration and it is very recently only that Deep Ray Therapy has been restarted and hence no cases under this group have been included in our consideration. However, we trust, some of you will be able to present the subject from this angle and so help us to complete it.

Etiology—The efficient cause lies beyond the irritation or injury which are but partial causes of the disease. (1) Heredity, chronic irritation, excessive use and abuse of voice, abuse of alcohol, tobacco, syphilis have all been arraigned as predisposing causes. C Jackson attaches great importance to vocal abuse. The basic cause of malignancy is unknown and Jackson very clearly and briefly puts it into an algebraic formula

$$E = A + S + C + I + F + a + T + H + X + Y + Z$$

Where A means age, S means Sex, C for senile changes in epithelium, I for irritation, F for frustrated repair, a for alcohol, T for tobacco, H for heredity and X Y Z other unknown factors of which we know nothing about so far.

Heredity—There is no evidence that cancer is transmissible from parent to offspring but cancer susceptibility and cancer resistance can be hereditary traits. Moreover we have come across 3 individuals who developed cancer in different parts of body quite different from each other at different times, showing cancerous diathesis. So, it is quite possible that there may be a hereditary tendency in cancer.

Age—It is unusual below the age of 30 years and common between 40 to 50 years. In our series of 312 cases, we had 2 cases in the

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second decade period, viz at 13½ and 16 years of age Our oldest patient was 85 years old

TABLE I.—Age Incidence

	11 20	21 30	31-40	41 50	51 60	61 70	71 80	81 90	Total
Out patients		18	58	70	38	10	7	1	202
In patients	2	0	32	37	24	5	1		110
	2	27	90	107	62	15	8	1	312

Sex—Sex plays an important part in the incidence of the disease In our series, it was M F=10 1

TABLE II.—Sex Incidence

	10 20	21 30	31-40	41 50	51 60	61 70	71 80	81 90	Total
Male	2	24	75	103	37	14	8	1	284
Female		3	15	4	5	1			28
	2	27	90	107	62	15	8	1	312

Again, but for the post-cricoid site,—which according to C Jackson is 7 times as frequent in females as in males, cancer Larynx in females would be much rarer still About half of our 28 females cases were post-cricoid type

Classification—Because of the sparsely supplied and closed lymphatic drainage of the cordal area, in 1879 Krishaber named cancer arising from this area as intrinsic and growths arising elsewhere in the Larynx, viz, (1) ventricular bands and vestibule (2) epiglottis, ary-epiglottic fold and arytenoids (3) pyriform fossa (4) post cricoid—all these as extrinsic cancer Besides there is a third group—sub-glottic—where the growth originates below the cord and may extend and involve the true vocal cord later and hence is often not recognised till a late stage

96 per cent of cases are squamous called epitheliomas and very occasionally adeno-carcinoma (of ventricle), papillary carcinoma and basal celled carcinoma

In 54 cases, degree of malignancy was graded

TABLE III.—Grading

Grade	I	II	III	IV	Total
	1 2%	14 64%	17 24%	6 10%	34

Grade III and IV are radio-sensitive and being more malignant type are much more likely to give rise to local recurrence and meta-

stasis and hence, apart from intrinsic cases (where because of closed lymphatic drainage and slow growth, all grades are treated alike by Laryngo-fissure operation, Grade III and IV in any other part of larynx should always be treated by irradiation and these radio-sensitive type comprise about one-third of all cases

Diagnosis—Diagnosis of cancer depends upon

- 1 History
- 2 Indirect laryngoscopy Symmetry of larynx and equal movements of both sides, particularly of both cords should be noted
- 3 Palpation
 - (A) Laryngeal cartilages for any fullness or asymmetry
 - (B) Palpation of neck for lymph nodes
- 4 X-Ray examination of neck and chest
- 5 Direct Laryngoscopy It gives a better and more comprehensive view, the extent of lesion can be judged more accurately and inaccessible region like sub-glottic and post cricoid can be properly observed and it enables accurate section taking
- 6 Biopsy The final and most conclusive proof of all our deductions and suspicions is the histological report and it should be done in each and every case of suspected disease of the larynx It should be taken every time readily for confirmation of our findings and in case of large size growth, it should be taken from more than one position and preferably from the edge of the growth Biopsy helps not only to make a positive diagnosis but also it helps us to give some prognosis and plan the line of treatment i.e., if it is radio-resistant type, the operation and if it is grade III and IV i.e. more malignant and radio-sensitive type, then irradiation

Symptoms—Symptoms vary according to the site of origin and the extent of the lesion A small growth on the edge of the cord will cause persistent hoarseness whilst in a situation like ary-epiglottic fold it may reach a considerable size without symptoms and sometimes only a secondary deposit in a gland in the neck first attracts one's attention

A sub-glottic growth may cause nothing beyond a slight discomfort until it is large enough to interfere with breathing and speech. A growth in the epiglottis and post-cricoid region may readily cause dysphagia before it disturbs the larynx or affects the glands

Intrinsic Cancer.—The growth arises generally at the junction of the middle and anterior one-third, the two extremities are generally free in early cases It rarely arises primarily in the posterior third It extends along the whole length of the cord and may reach the anterior commissure and involve the interior end of the other cord—directly, or may become sub-glottic and then pass on to the other side without involving the anterior commissure Even when it infiltrates through the substance of the cord into the muscle the hyaline

cartilage of the thyroid wing presents an effective barrier for a long time before it can come to the surface and involve the prelaryngeal muscles. Symptoms, although trivial, cannot be missed. It is just voice fatigue, towards the end of the day. Then there is hoarseness, slight at first, and then more marked. The symptoms are persistent and progressive and even if the patient himself remains indifferent, people around, will notice the change in his voice. As it progresses, the increasing hoarseness would amount to aphonia, and as the lumen of the glottis is encroached upon, dyspnoea and stridor slowly develop. By this time, if the growth would have grown beyond the intrinsic barrier it will advance rapidly and will carry the prognosis of extrinsic cancer. The rate of growth so far has been very slow, so that the span of life in an uninterfered with case of intrinsic cancer is as long as three to seven years.

Extrinsic Cancer—The symptoms are vague, insidious and uncertain. Unlike the intrinsic, the symptoms are not noticeable to others, who would draw the patient's attention, even if the patient was indifferent. Sometimes, metastatic deposit in the glands of the neck may come up before the patient complains of any discomfort in the larynx. The vague symptoms are local discomfort, feeling of something foreign sticking in the throat, in spite of constant hamming efforts to throw it out, increased salivation, difficulty in throwing out or swallowing down saliva which becomes very thick, and then increasing dysphagia. The symptoms are primarily concerned with deglutition. The discomfort increases to pain. The pain radiates to the jaw or the ear, and is increased on swallowing. The progress is rapid and the span of life is six months to eighteen months. Glands readily appear, the growth invades the larynx, voice gets muffled, dyspnoea and stridor may appear. As the growth ulcerates and fungates, foul breath, sloughing, haemorrhage, wasting and infection of the lower respiratory tract bring about a rapid end. Perichondritis and necrosis of the cartilage may occur. Early case of post-cricoid cancer in spite of definite symptoms may be overlooked, sometimes in spite of direct laryngoscopy. In subglottic variety, sometimes it is difficult to take an appropriate biopsy or to judge its full extent. Early diagnosis in intrinsic cancer offers every promise of a lasting cure which is round about 80 per cent. But in extrinsic cancer which in early cases gives some vague symptoms only and which as it arises in free lymphatic drainage area advances rapidly, the prognosis is as bad as any other part of the oropharynx. However, some of our advanced cases have given us encouraging results, much beyond our expectation. Most of our cases come in a very advanced stage, so that we come across extrinsic cancer as a rule and intrinsic cancer just occasionally as an exception. In our series of 312 cases only 16 cases were truly intrinsic and could have been treated by the conservative type of operation. This impression of extrinsic being so much more common than intrinsic $E:I=20:1$ may be to some extent misleading. In more recent cases (42) where extrinsic which have originated as in-

trinsic and so were considered intrinsic gives ratio of 10 1—E I Many of these perhaps, began as intrinsic and later became extrinsic But still a great many more must have begun as extrinsic, as there would be a large growth in extrinsic area and yet movements of the cord would be just impaired, i e, intrinsic area being secondarily involved In my private practice series of 103 cases of cancer larynx that came under my observation in the last 5 years (mainly for opinion and for one observation and where generally no section was taken and hence this series not included in our Hospital series) there were 87 males to 16 females M F=11 2 The proportion of intrinsic to extrinsic was 39 to 64 As far as extrinsic cancer is concerned, as the lesion was in advanced condition and with marked symptoms and secondary glands, there could not be much doubt about diagnosis However, all doubtful cases of early intrinsic cancer and may be cases other than intrinsic cancer have been included Still this series shows extrinsic almost twice and probably more than twice as common as intrinsic In Western countries it is the reverse of this This has got a very weighty bearing on prognosis, line of treatment and cure

Treatment—As far as intrinsic cancer is concerned, there is no divergence of opinion as to treatment It is always laryngofissure operation even when the growth belongs to grade III and IV It has given cancer cure of 5 years and over in about 80 per cent of cases

Unfortunately, this type of cases are very rare for us Partly because our cases come at a very advanced stage but also because this is the unusual rather than the usual type of cancer Larynx, amongst us and this view was upheld by representative members from different parts of India at the Fifth Annual Conference of the Association of Surgeons of India The 80 per cent of cancer cure results is claimed if the patient really comes early before any infiltration and limitation of movements of cords takes place Even when limitation of movements or fixation has occurred i e, the case has been neglected for 1 to 3 years and more, still laryngofissure operation would give as much as 45 per cent cures, if the growth remains confined to the intrinsic area Even in cases of slight extension into subglottic area or beyond the anterior commissure to the opposite side, Jackson's laryngofissure operation slightly modified holds good Here, after cutting just through the thyroid cartilage, subperichondrial dissection is done, both towards less and more diseased sides and then the lumen of the larynx is entered into, from the less involved side and then the commissure and more diseased side, all are removed in one piece, without at any time cutting into the growth Clef removes a wedge of thyroid cartilage also

For advanced cases of intrinsic cancer which have encroached upon either the subglottic area to more than a trivial extent or have encroached upon the vestibular or arytenoid region and with no involvement of glands, narrow-field laryngectomy should be done and all cases of laryngectomy in Americans fall in this category Out of our 38 patients only 3 were suitable for this type of operation Be-

cause of the preservation of good blood supply and retention of muscles to reinforce the suture line healing takes place practically by first intention. A midline incision from the upper border of the hyoid bone to the jugulum is made. No structure is come across except the thyroid isthmus which is cut across and retracted. Our object is to remove the larynx and as little else as possible. So the muscular attachments of the prelaryngeal muscles in the thyroid cartilage are separated or better still the external perichondrium of the thyroid cartilage is raised up from the cartilage with the muscles attached to it. After mobilising the laryngeal box from in front the whole larynx is tilted forcibly to one side so as to bring into view the superior and inferior cornua, the superior cornu is clipped off so as to help full rotation and the superior laryngeal vessels and nerve are sought for on the posterior end of thyrohyoid membrane and ligatured. Same way the inferior laryngeal artery is sought following the posterior edge of the thyroid wing. After mobilising the larynx from its sides, the pharynx is entered through the thyrohyoid ligament. Mucous membrane lining the pyriform fossa along with the underlying muscle is shaved away from the signet part of the cricoid. This leaves ample mucous membrane to reconstruct the pharynx without any tension and the prelaryngeal muscles over it reinforce the suture line and prevent any leakage. Practically no vessels are cut across except the superior and inferior laryngeal vessels, the blood supply of the parts is good and healing, almost by first intention may be expected.

The majority of our cases (33) were beyond the larynx into pharynx i.e., involving aryepiglottic fold, pyriform fossa, or post cricoid region and here widefield laryngectomy was essential. Here broad flaps of skin were to be planned (I, U, V, T, shaped). The prelaryngeal muscles have to be dissected out. The carotid sheath is explored and glands dissected out. Because of infiltration of the soft structures, the superior thyroid artery rather than superior laryngeal may have to be ligatured. The pharyngeal muscles are detached from the posterior edge of the thyroid cartilage. After this wide exposure the pharynx is entered into, the limits of encroachment on the pharynx is defined and the larynx along with involved part of the pharynx is removed. This means only a segment of the pharynx is left behind. This is sutured over a catheter passing into the oesophagus. There is considerable tension on the suture line, tissue planes are widely opened into, blood supply is poor, no muscles to reinforce suture line and prevent leakage and breaking down of the suture line, and pharyngostome results. Six of our 15 post-operative deaths resulted from sepsis and secondary haemorrhage due to leakage. The convalescence becomes very trying and prolonged and plastic colours for pharyngostome was required in half the number of cases.

In our series of 312 cases only 16 cases were considered suitable for laryngofissure and only 4 out of these came for operation. The rest 296 were advanced enough to need laryngectomy or were beyond it.

Out of these, 38 consented to laryngectomy and only 3 were suitable for narrow-field laryngectomy. In 33 cases widefield laryngectomy or pharyngo-laryngectomy was done. The lateral pharyngotomies were done.

In all 4 laryngofissure operations, the thyroid cartilage was split in the middle. In one of those cases, the growth had involved the anterior end of the opposite vocal cord and so was really suitable for C Jackson's modification operation. Of our 4 cases one died of hemiplegia 6 months after operation and one was found out to be tuberculoma of the vocal cord (where the first section was not adequate and a second section asked for, but was not purposely taken and where repeated sputum examination and chest findings were negative). The two remaining cases could be traced only for one year.

The three cases of narrow field laryngectomy were really neglected cases of intrinsic cancer, where the growth had extended into subglottic or vestibular regions but still well within the cavity of the larynx and there were no glands.

The remaining 33 were widefield laryngectomies where the growth had involved epiglottis, ary-epiglottic fold, pyriform fossa, or post-cricoid region or involvement of perichondrium and with involvement of glands in many cases. Here along with larynx, part of pharynx had to be removed. Tapia, VanGluck, Sorenson have referred to series of laryngectomies by the hundred and it is mainly the narrow-field laryngectomies. In a series of 250 cancer larynx operated cases by Clerf there were 149 laryngofissures. 86 of these were done over 5 years back, 66 i.e. 77 per cent had no recurrence.

Of the 101 laryngectomy patients 52 were done 3 years back and over. Out of these 53 per cent were free from recurrence 3 years and more after operation and 40 per cent were free from recurrence 5 years and more after operation. These again include narrow-field operations only. The other cases coming out of the larynx and involving part of pharynx which could have been operated by wide-field laryngectomy were considered inoperable and treated by irradiation by Coutard's method of fractional irradiation and they obtained 24 per cent 3 years and over cures (4 out of 17).

Of our 33 cases suitable and operated upon by wide-field laryngectomy 18 came through their convalescence. Out of 32 patients reviewed 2 years back, 9 were traceable as alive for 3 years and over i.e., 28 per cent and one of these 9 has come back recently with local recurrence, 5½ years after operation. Another of these 9 had come back 11 years after with a second primary in the tonsil. Tonsil was removed and the bed irradiated and there was a year after a third primary or recurrence in the posterior one third tongue opposite side. Patient was again irradiated 1 year back and is so far well. Now his brother has come with inoperable cancer larynx.

Of the 2 lateral pharyngotomies, one has come back 5½ years after with no recurrence and a second primary cancer on the cheek, opposite side. The second case died of secondary haemorrhage.

Operative Mortality—Laryngofissure is considered a comparatively safe operation and the operative mortality may be round about one per cent. The same cannot be said about laryngectomy which is a much more severe and traumatising operation and where because of bronchial complications inability to cough out properly, the operative mortality correspondingly rises. In narrow field laryngectomy 5 per cent and in wide field laryngectomy 15 per cent of operative mortality has been estimated. In our first 32 cases the operative mortality was as high as 47 per cent whereas in the last six consecutive cases there has been no mortality. We can also hope to keep it assuringly low by proper pre-operative treatment including blood transfusion (as because of dysphagia our patients are in a very low stage of nourishment and practically dehydrated) and by preventing post-operative pulmonary complications by exclusive use of (1) local anaesthesia (2) preventing blood during operation from reaching the tracheo-bronchial tree by efficient aspiration and (3) by getting rid of post-operative secretions by keeping a suction pump by the side of the patient's bed during his early convalescence.

Irradiation—We have no independent experience of irradiation therapy. Whatever cases that have been irradiated primarily have not lived over 3 years.

For cordal cancer, whatever the grading when laryngofissure can claim 80 per cent 5 years and over cure, there is no place for irradiation. For extrinsic cancer in grades III and IV recurrence is much more frequent and the growth is radiosensitive, so whether the growth is within the cavity of the larynx or in the pharyngolaryngeal region with or without glands, irradiation is the method of choice. These constitute about 33 per cent of our cases. But the remaining 67 per cent are the radio-resistant type and should do better with laryngectomy. Our present day practice is to do in such cases laryngectomy first and give prophylactic post-operative radiation afterwards particularly when we are not happy about having removed the growth with a comfortable margin of healthy tissue. Palliative radiation i.e. radiation in smaller doses is very helpful in easing of the sufferings of inoperable cases.

Dr Paymaster said. In the first 3 years, out of a total of 5,000 cases recorded there were 3,900 cases of cancer. The rest were non-cancer problems. Cancer of Larynx was recorded in 404 cases, 10.3 per cent of all cancer cases.

Cancer of the Extrinsic Larynx was present in 371 cases—91.2%

Cancer of the Intrinsic Larynx was present in 33 cases—8.8%

At the Memorial Hospital New York it is 7.4 and 20% respectively.

The classification followed at the Tata Memorial Hospital was the one suggested by Dr. Hayes Martin of the Memorial Hospital New York.

There were 376 males—93% and 28 Females—7%.

Classifying them according to the communities—

Hindus 282—65% (Gujaratis 144 and Deccanites 118)

Mohamedans 101—25% and other communities 41 cases—10%

70% of the cases recorded had metastasis in the neck. 5% more developed metastasis during or soon after the treatment was completed.

In a series of 500 cases of cancer of the tongue 92% of the cases had metastasis.

Main Symptoms —Lump in the neck was noticed in 70% of cases
 Hoarseness of voice was noticed in 10% of cases
 Soreness in the mouth or difficulty in swallowing was noticed in 20% of cases
 The average time that elapsed between the appearance of the first symptom and the patient's visit to the hospital has been calculated as nine months. The average age of the patient was 45 years.

Causative Factors —1 Heavy smoking has been recorded in over 80% of cases
 2 Bad teeth were present in almost all cases
 3 Excessive use of voice has not been properly recorded and thus cannot be evaluated.

4 Syphilis as judged from a positive Kahn test was recorded in 10% of cases

Pathology —314 cases had definite histological evidence

Squamous and epidermoid	grade 1	— 15
"	grade 2	— 175
"	grade 3	— 72
carcinoma ungraded		— 52

Treatment —Intrinsic cancers of Larynx are radio-resistant and being of lower grade malignancy are best suited for surgery

33 Intrinsic cancer cases were treated as follows —

20 by surgery
 5 by X radiation
 2 by X radiation and Radon seeds and
 6 cases either took no treatment or incomplete treatment

Out of the 20 cases treated by surgery 11 were total Laryngectomies
 8 were partial Laryngectomies
 1 was total Laryngectomy plus X radiation

There were 4 Post-operative deaths (3 in the total Laryngectomy group, and 1 partial Laryngectomy)

Five total Laryngectomy cases are traced well and without any evidence of any disease for a period of 2½ to 4 years

Seven partial Laryngectomy cases are well and alive for a period varying from 2½ to 4 years

Dr Paymaster then asked Dr Gandhi a few questions. He was interested in knowing how many Extrinsic Larynx cases Dr Gandhi had operated upon. He also wished to know whether Dr Gandhi did a radical neck dissection or simply excised the nodes in the neck with the larynx also if the operated cases were followed by deep X radiation.

Dr K P Mody in the course of his remarks said that it was a misconception that in foreign clinics cases of Intrinsic Larynx were far more than those of Extrinsic Larynx. He quoted figures from the New York Memorial Hospital and from Boston proving that Extrinsic Larynx cases were 4 times as many as Intrinsic. At the Tata Memorial Hospital these cases were 8 times as many. One reason for this great preponderance was that patients with Intrinsic lesions came for treatment very late when the disease broke down the barriers and involved the extrinsic structures the intrinsic-extrinsic group. The more important reason was derived from a comparison with the tongue group. The base of the tongue was far more predominant than the anterior two thirds. The mucosa of the base of the tongue was continuous with the extrinsic larynx structures and hence the same factors which produced the one produced the other. He controverted the statement of Dr Gandhi that radiation treatment had no place in Intrinsic Cancer. Workers of the eminence of Coutard, Pfahler, Lenz, Quick obtained excellent results with deep X rays in this location. But he agreed that operation for cord lesions was simple and effective and so there was nothing to be gained by submitting the patients to a prolonged course of treatment and that was the practice adopted at the Tata Memorial Hospital. In more advanced lesions where the operation had to be total laryngectomy, some patients would hesitate to submit to operation and lead a life of a dumb animal. Artificial voice boxes were not so convenient and many patients could not get used to them. In such cases radiation was a valuable substitute. He maintained that extrinsic larynx lesions were essentially radiological problems. These were radio-sensitive lesions and were amenable to such treatment. So far the results even in such highly specialised clinics as the New York Memorial Hospital were disappointing. Their results were 9%. The one important reason for such poor salvage was the very poor material they had to deal with and that is also the experience at the Tata Memorial. He pointed out that out of 25 cases undergoing treatment at the present time 21 could be written off straight away being advanced problems. He considered involvement of the Pyriform, the arytenoids, metastasis to glands, extension to base tongue and those requiring tracheotomy very grave conditions with practically no salvage possible.

He said that the treatment should be given daily beginning with small doses and gradually working up to a high total. High K V and high filtration were desirable. One thorough course should be given and not repeated.

He then stated the results obtained in his department at the Tata Memorial. In 1941 out of 42 cases who had received complete treatment, 12% survived for 3 and 4 years free from disease. In 1942 out of 44 cases, 8 survived from 2½ to 3½ years free from disease—18%. In 1943 34 cases received treatment and 8 cases survived from 2 to 2½ years a salvage rate of 23%. In conclusion he expressed the hope that a time may come when early diagnosis would permit much better results.

Dr P V Gharpure pleaded for co-operation between the various institutions in elaborating a scheme for a systematized study of tumours.

Dr H D Gandhi replying said that in all cases of wide field Laryngectomies whether the glands in the neck were palpable or not, these glands were looked for systematically when the carotid sheath was exposed. It has been found out that in some cases the glands

were involved even though they were not clinically palpable. He further added that pre-operative irradiation is a contraindication although there is a tendency in some quarters to give an initial small course of 3,000 m.c. in 10 to 14 days time and if the growth reacted favourably as judged by the loss of fixation and diminution of size then the full dose i.e., 6,000—7,000 m.c. is given. If however the growth does not prove to be radio-sensitive then the operation is performed after an interval of 3 weeks. Post-operative radiation is desirable specially when the growth was found to be more extensive than expected and when accompanied by a mass of glands. In the series quoted post-operative radiation was given in four cases done latterly.

In all cases of Intrinsic cancer of the larynx irrespective of grading, the choice is operation and this is laryngofissure where the operative risk is 1 per cent and the voice is preserved. Operation is the method of choice and many different workers claimed cancers cured (above 5 years and over) as much as 80 per cent.

For extrinsic cancer which belong to Grade I and II and which are operable by narrow field laryngectomies, cancer cure was claimed to be 40 to 45 per cent. In his extensive type of cases which required wide field laryngectomies cancer cure was 28 per cent and these compare favourably with irradiation results only. However, these were different methods and they have to be adopted according to various circumstances besides the location, extent and grading of the growth. The patient's own reaction has to be considered as regards his physical condition, age and life expectancy independent from the occurrence of cancer.

He further remarked that the co-operation and impartial deliberation and judgment between the Radiologist and the Surgeon was necessary as aptly pleaded by Dr V. R. Khanolkar.

THE ASCHEIM-ZONDEK TEST IN THE DIAGNOSIS OF TUMOURS*

by

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The appearance of the gonadotropic hormone of the anterior hypophysis in the urine of a man suffering from teratoma testis was first observed by Zondek (1929). Two years later, Fergusson and his associates reported their preliminary findings, based on a study of 12 cases, on the use of the Ascheim-Zondek test in the diagnosis of teratoma (1931). They observed that irradiation caused a fall in the hormone output. This study was followed by a more extensive report by Fergusson (1933) giving the data on the quantitative behaviour of prolan A in teratoma testis after a study of 117 cases by means of 1000 biological tests of the urine.

Zondek has shown that prolan A, or follicle-ripening hormone is responsible for the productions of reactions I and II in the ovary of an immature mouse. Prolan B is the luteinizing hormone and is responsible for the formation of the corpora lutea in the ripened follicles. Reaction I consists in hyperemia and swelling of the Graafian follicles together with the formation of a cumulus oophorus. In reaction II, massive hemorrhages are found in the ripened follicle. The formation of corpora lutea constitutes reaction III. He has further shown that prolan A and prolan B occur in the urine of pregnancy approximately in the ratio of 5:1. This quantitative relation of prolan A and prolan B also holds in the urine of male suffering from teratoma testis.

It has been proved repeatedly by Fergusson (1933) in his series of 117 cases that when a given number of units of prolan B is found, mice injected with the equivalent of $1/5$ as much urine will show reactions I and II, a conclusive proof of the presence of prolan A. On this basis, the total content of hormone in the urine is calculated in terms of mouse units of prolan A.

Twombly (1944) expressed his opinion that because the nature of the gonadotropic hormones was not well understood at first, certain errors have crept into the literature on the subject and have caused great confusion. Hamburger (1933) was probably the first to demonstrate clearly the difference in the reactions produced by pregnancy urine and urine from castrates or women past the menopause. Two different kinds of hormone were differentiated, the chorionic type (pregnancy urine, pregnancy blood, placenta, chorion-epithelioma) and the hypophyseal type (anterior pituitary lobe, castrate blood, normal male and female urine, castrate urine, urine of carcinoma).

* This work was carried out under the guidance of Dr A. R. Khanolkar, Director of Laboratories.

patients, blood of pregnant mare, urine of women past the menopause) Evans and his co-workers studied the type of hormone excreted by a patient with teratoma testis and came to the conclusion that it resembled that found in pregnancy urine in some respects and anterior pituitary extracts in others Zondek (1941) assumes that in the anterior lobe a special additional hormone is elaborated (synergistic factor) which if added to prolán, induces in this substance the same activity as is exerted by the hormone from the anterior lobe Zondek has chosen the following terminology the hormone of the chorionic type is called prolán, the synergistic factor is called synprolán, the hormone of the hypophyseal type (prolán and synprolán) is called prosylán Since he adhered to the theory that the gonadotropic hormone contains two different factors, the follicle-ripening factor (A) and the luteinizing factor (B), he further differentiates between prolán A and B and, accordingly, between prosylán A and B

It was noted by Fergusson (1933) that untreated tumours of approximately the same size or with the same extent of metastatic spread excreted different amounts of hormone He therefore suggested that the amount of hormone excreted depended upon the morphological type of the testicular tumour and described the following definite levels as characteristics of the histologic varieties

TABLE I.—Level of gonadotropic hormones in Tumours

Type of tumours	M U of prolán A per liter		
Choriocarcinoma	40 000	or	more
Embryonal adenocarcinoma	10 000	to	40 000
Embryonal carcinoma with lymphoid stroma	2 000	to	10 000
Seminoma	400	to	2 000
Adult teratoma	50	to	500

With regard to these levels Fergusson (1934) stated that, 'the limits reached by each type of tumour overlap so little that it is possible to make the diagnosis on the basis of this determination alone' But Twombly (loc cit) observes, this has proved only partially true More extended study has shown a tendency for the more malignant embryonal adenocarcinomas and chorioepitheliomas to excrete larger quantities of the chorionic type of gonadotropin, but many exceptions are found, widespread adenocarcinoma showing very little or no hormone, while some embryonal carcinomas (seminomas) show large amounts

Hamburger, Bang and Nielson (1936), in trying to correlate gonadotropic hormone excretion with the histologic appearance of the tumour, have laid emphasis on the type of hormone rather than its quantity They divided their cases into three types (1) Mixed epithelioma (2) Seminoma and (3) Polycystic teratoid mixed tumours, and maintained that the first was radio-resistant and excreted the chorionic type of gonadotropin while the second and third excreted

the castrate type, follicle-stimulating hormone Seminomas excreting follicle-stimulating hormone were radio-sensitive

Furuhjelm (1941) reported that out of 28 seminomas, 7 did not excrete any measurable quantity of hormone, 12 excreted follicle-stimulating hormone, 5 chorionic gonadotropin, and 4 both types of gonadotropin Out of 7 malignant mixed epithelioma, 6 excreted chorionic gonadotropin and 1 the castrate type of gonadotropin, follicle-stimulating hormone

Twombly (1944), from a study of 135 testicular tumour cases, reported that the gonadotropic hormone had been looked for in the urine in 63 cases He found the following results as given in the table below

TABLE II.—Gonadotropic hormone in testicular tumours

	Chorionic gonadotropic hormone	Follicle stimulating hormone	No Gonadotropic hormone (below 50 to 100 m u per day)
1 Chorionepithelioma	~	2	
2 Embryonal adenocarcinoma	10		1
3 Embryonal carcinoma with lymphoid tissue (seminoma)	0	-	-
4 Tumour showing mixed characteristics of 2 and 3	1	1	
5 Adult cystic teratoma		3	
6 Complete destruction by γ rays	2	1	3
7 No report	7	2	1
Total	38	18	7

From these results the author remarked that one cannot tell surely the histologic type of tumour by the type of gonadotropic hormone found in the urine However, in general all agree that the chorionic type of hormone is more typical of adenocarcinoma (mixed epithelioma of Hamburger) while the castrate type of hormone is apt to be associated with seminoma (with frequent exceptions)

Recently Twombly, Temple and Dean (1942) have presented data after a detailed study of 203 cases of testicular tumours They performed the quantitative Ascheim-Zondek tests according to the method of Fergusson Their study revealed little co-relation between the amount of gonadotropic hormone found in the urine and the histologic type of the tumour Further, in only 47 out of 155 cases in the series followed by serial tests was there any close co-relation between the hormone level and the clinical course of the disease They therefore expressed the opinion that obviously a test which in only 47 out of 155 serial determinations shows close correspondence with the condition of the patient is of little clinical value According to their view the failure in co-relation may be ascribed to the inadequacy of the test as originally described They think that if the modifications they have suggested are adopted a number of errors in the former technique may be corrected

In this hospital the test is carried out according to the technique of Fergusson as follows. The sample from 24 hours' collection of urine is assayed on five infantile mice. The sixth mouse is kept as a control, no injections being given to it. The ovaries are examined with a hand-lens for the chorionic type of gonadotropin, the reactions (APR) II or III being looked for, as Zondek (1942) has stated that reactions II and III are given by prolactin B. The values of the hormone content are calculated directly on this basis of the examination of the ovaries, that is, in terms of the chorionic type of the hormone, instead of in terms of prolactin A after multiplying these values by five. In case the urine is found to be toxic to the animals, the hormone is precipitated by alcohol and the test is carried out by redissolving the precipitate in distilled water in aliquot quantities.

The total number of determinations so far done, is 45 on 35 patients. Out of these 35 patients only 16 cases provided a suitable basis for a study of the co-relation between the amount of the hormone in the urine and the histologic structure of the tumour. The data has been presented in the following table.

TABLE III.—Level of prolactin B in tumours

Histologic type	Number of cases	Prolactin B. Mouse units per liter	Extent of disease	
			Localized	Advanced
1 Teratoma	6	250 or less than 250	4	2
2 Seminoma	—	200 or less than 200	1	1
	1	480	—	1
	1	3,000+	—	1
3 Embryonal carcinoma with lymphoid tissue	1	less than 80	1	—
4 Embryonal carcinoma	1	500	1	—
5 Chorioepithelioma	1	2,000 to 10,000	1	—
	1	30,000+	1	—

Out of a total of 16 cases, 6 were teratomas having the excretion of 250 or less than 250 mouse units of prolactin B per liter, 4 were seminomas out of which two excreted 200 or less than 200 mouse units, one 480 mouse units and the fourth one with the excretion of more than 3,000 mouse units, one was embryonal carcinoma which gave the value of 500 mouse units, 1 embryonal carcinoma with lymphoid stroma had less than 80 mouse units, and 4 were chorioepitheliomas out of which 3 had a level between 2,000 to 10,000 mouse units and one showed more than 30,000 mouse units per liter. Thus it will be seen that the same difficulty arises in this data in co-relating the amount of gonadotropin present in the urine with the histologic type of the tumour, as was experienced by many other workers and we are in essential agreement with their views.

The modifications suggested by Twombly et al (loc cit), however, are worth considering, in spite of the generally expressed pessimistic views of most workers. There is one further consideration which may be borne in mind in the case of future studies on the subject. So far

no mention has been made by the investigators in their report about the strain of mice used for the test. We have been using Haffkine strain of mice in our tests throughout the experiment. From the studies by Hummel (1942) it appears that there are differences in the response by different strains of mice to extracts of human pregnancy urine. About 11 different strains of mice were used during the investigation and it was found that the A strain showed considerably less while the C57 brown and C57 leaden considerably more response than the other mice. Thus it can be mentioned that perhaps this strain difference might be one of the many unknown factors causing the discrepancy in the co-relation of the biological assay of the gonadotropin and the histological findings. It will be, therefore, worthwhile to study if any co-relation could be obtained after eliminating this factor by choosing a suitable strain of mice and using the same one throughout the experiment. It may be interesting to determine the difference in response of mice of different strains to gonadotropic hormone in urine from patients of testicular tumours, in similarity to the difference found in case of human pregnancy urine.

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Medical News & Notes

MYCOBACTERIUM LEPRAE (BACILLUS LEPRAL, HANSEN, 1874) IN CULTURE AT LAST—We are glad to announce the successful culture and subculture of this mycobacterium in the Laboratory of the P G Singhanee Hindu Hospital by our veteran worker Dr R Row, DSc, M.D (Lond), the Hon Director and Consulting Physician, P G Singhanee Hindu Hospital, Bombay. Although the preliminary report is sent up for publication elsewhere, we feel we have been privileged to make the announcement of this important discovery and we hope to refer to the subject shortly. Many investigators in the past have claimed cultures from the lepra nodules but none of these has been accepted beyond doubt as true leprosy bacillus. The last claim was that of McKinley and Soule. When Dr Row's discovery is confirmed and accepted as true leprosy bacillus capable of causing experimental leprosy, we have no doubt it will open up new vistas for bacteriologists, chemo-therapists and clinicians, in fighting this dread scourge of India. Our homage to Dr Raghavendra Row for the true scientific spirit and tenacity with which he has persisted in his lone search for many years!

ELECTRIC CONVULSION THERAPY APPARATUS—The value of electric convulsion therapy in psychiatric practice is now well-established, though the rationale of its use is not understood and the field of its application is limited. The difficulty of obtaining the apparatus in India has been overcome by the Shakti Electric Mfg Co of Bombay, who has built and put on the market a handy, lightweight, simple apparatus operating on a.c. current and delivering a current of 60 to 120 volts for 0.1 to 0.9 second. The voltage intensity and the time duration can be varied by an electronic device. The editor has used this apparatus in his practice for the last six months without any difficulty and has found it easy to operate, safe and fool-proof. It can be readily recommended to all institutions and practitioners interested in the treatment of the mentally ill.

THE ASSOCIATION OF PHYSICIANS OF INDIA—The First Conference of the Association of Physicians of India will be held in Bombay on the 20th and 21st of April, 1946. Those who hold post-graduate degrees or diplomas in Medicine, Psychiatry, Dermatology, Pathology, Bacteriology, Radiology, or Physiology and are engaged in consulting practice, or are teachers in these subjects are eligible for election as Members of the Association. Those eligible for Membership are requested to attend the Conference and if possible to contribute papers. The paper should not ordinarily take more than twenty minutes to read. A summary of the paper should reach the Secretary by the 9th March 1946 and two typewritten copies of the paper should reach him by the 30th March, 1946. For further particulars, please write to Dr J C Patel, Secretary, Scientific Subcommittee, Back-Bay View, New Queen's Road, Bombay 4.

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Original Contributions

CRUVEILHIER-BAUMGARTEN SYNDROME

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Cruveilhier (1852) observed a well marked thrill and a loud murmur in the epigastric region in a case of portal hypertension with extensive collateral circulation and splenomegaly. Post-mortem showed widely patent umbilical vein, small and atrophic liver and an enlarged spleen. He thought that patency of umbilical vein was the primary condition and atrophy of the liver secondary. Baumgarten (1908) observed exactly similar clinical and post-mortem findings in another case and came to the same conclusion that patency of the umbilical vein was the primary condition and changes in the liver secondary. Thayer (1911) had observed this murmur in cirrhosis of liver in a fairly large number of cases. Hanganutz (1922) reported six cases of persistent umbilical vein and called the condition Cruveilhier-Baumgarten cirrhosis. Florand (1922) described a case in which a continuous bruit was heard over the dilated veins of the abdomen but more prominent at the lower end of the sternum. Hatzieganu and Sharteu (1924) observed a venous hum over the dilated veins of the collateral circulation in a case of portal thrombosis. Kelly and Vincent Lyon (1926) observed a venous murmur over the dilated veins in the epigastrium in the collateral circulation of cirrhosis of the liver. Roleston and McNee (1929) noted that in some cases a thrill and murmur may be heard over the epigastric region in cases of cirrhosis of the liver with abnormally dilated veins. The murmur was more prominent during inspiration, may be heard at the umbilicus and may diminish or completely disappear after tapping but reappear when the fluid reaccumulates. They reported the case of a man aged forty-three in whom a continuous murmur was heard over the epigastrium and on post-mortem showed advanced cirrhosis of the liver and a large veins in the falciform ligament. Armstrong et al (1942) who reviewed the literature of this syndrome, found 52 cases and added three more of their own. Valk and Horne (1942) reported a case of Cruveilhier-Baumgarten syndrome with portal hypertension, patent umbilical vein and splenomegaly. Wollaeger and Shands (1945) reported the occurrence of this syndrome in one of their cases of

Wilson's hepatolenticular degeneration, in addition to the neurological signs. Well marked collateral circulation was seen in the upper part of the abdomen and lower margin of the thorax. A continuous venous hum was heard over these dilated veins and the murmur was recorded by cardiophone.

A brief summary of the two cases observed by the senior author is given below.

Case 1—A Hindu male aged 40 years was admitted in the hospital in June 1938 for ascites and oedema of the legs of four months' duration.

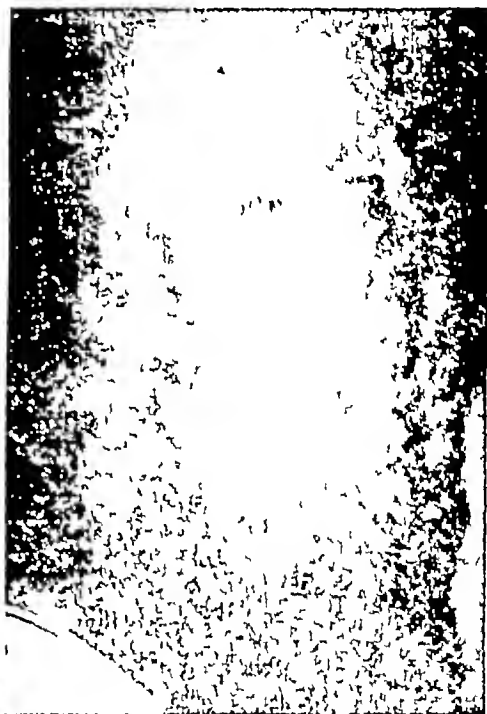


Fig 1 Showing the abnormally dilated and tortuous veins over the anterior abdominal wall more prominent in the epigastric region (Case 2)

Fig 2 Showing the abnormally dilated veins on the right side (Case 2)

Physical examination revealed the typical clinical picture of atrophic cirrhosis of the liver. The additional features were (1) abnormally dilated and tortuous veins extending from the umbilicus to the ensiform cartilage, the flow of blood being from below upwards, (2) a continuous venous murmur heard in the epigastric region just below the level of the ensiform cartilage. Another soft murmur was present at the lower end of the dilated veins. Radiological examination of the heart and lungs did not reveal anything abnormal. Blood Wassermann was strong positive. A clinical diagnosis of cirrhosis with Cruveilhier-Baumgarten syndrome was made. The patient was discharged at his request and he could not be followed further.

Case 2—R P Hindu male aged 34 years was first seen by the senior author on 1-10-1944. He gave a history of anaemia, dyspnoea on exertion, and prominent veins over the abdomen of eleven years' duration, the symptoms being more pronounced and the dilatation and tortuosity of the veins more prominent at the time of admission into the hospital. He was a married man with an only son of 12 years, gave a history of gonorrhoea ten years ago but none of syphilis. The complaint originally started eleven years ago with diarrhoea which persisted for about five months. Later he was treated for 'enlarged liver' with indigenous drugs. Physical examination showed a fairly nourished individual with slight anaemia and tortuous veins over the



Fig 3 Radiogram of chest showing enlargement of heart with hypertrophy of the left ventricle (Case 2)

abdominal wall. Spleen and liver were both palpable below the costal margin. Circulatory and respiratory systems were normal. A loud continuous murmur was heard over the dilated and tortuous veins at the lower end of the sternum better heard in the lying down than in the erect posture. Deep inspiration and stoppage of the respiration had no effect on the venous hum. No further investigation was possible since he had to leave the place for some urgent business.

He came back on 13-10-45 and was readmitted for further investigation. This time anaemia was more marked and dyspnoea more pronounced. Physical examination showed pallor, yellow colouration of the conjunctiva, and oedema of the legs. Abdomen was prominent with free fluid in the peritoneal cavity, spleen enlarged one and a half inches below the costal margin, and liver palpable on deep inspiration. Two abnormally dilated and tortuous veins were seen, one in the middle and the other on the right side of the abdomen and chest (Figs 1, 2). The loud venous bruit at the lower end of the sternum was more pronounced and was better heard in the lying down than

in the erect posture Neither inspiration, expiration or stoppage of the respiration had any influence on the intensity of the murmur Heart was slightly enlarged with systolic murmur in the mitral and pulmonary areas Respiratory and nervous systems were normal Examination of the eyes showed nothing abnormal Kayser-Fleischer rings were specially looked for and were not present

Radiological examination of the heart showed slight enlargement with left ventricular hypertrophy (Fig 3) and barium in the oesophagus did not show any definite evidence of varicosity of veins at its lower end

Blood pressure		Arm	Right	Left	
			130/80	125/80 mm Hg	
		Leg	140/90	140/90	
Blood	R B C	2 3 millions	W B C	3 800 per c mm	Differential count
	Polymorphs	75%	Lymphocytes	19%	Monocytes 2% Eosinophils 4%

Smear showed the picture of microcytic anaemia

Van den Bergh reaction was direct positive delayed, quantity too small for estimation

Blood urea	36 mgs per 100 c c	
Laevulose tolerance test		mgs
Blood sugar before giving laevulose		92 0
½ hr after giving 40 gms laevulose		107 5
1 hr		110 0
1½ hrs		121 2
2 hrs		103 1
Urine	Laevulose	
	Nil	
	Trace	
	Trace	
	Trace	

The test showed normal liver function
Blood Wassermann negative

DISCUSSION

Cruveilhier and Baumgarten (loc cit) after whom the syndrome is named independently described the abnormally dilated and tortuous veins in the epigastrium and continuous venous hum over the dilated veins After post-mortem examination they came to the same conclusion, that the murmur was produced by the collateral circulation between the portal and umbilical veins, that the abnormally dilated umbilical vein was congenital and the primary condition, and that the atrophy of the liver was secondary Subsequent observers Hagahutz, Florand, Hatzigianu (loc cit) and others have gone into the whole question and have come to the opposite conclusion that atrophy of the liver was the primary condition and the abnormally dilated veins secondary

The loud venous bruit that is heard over the epigastrium is due to the passage of blood from the portal vein through the falciform ligament into the veins of the anterior abdominal wall or the left internal mammary vein as in the case of Rolleston and McNee (loc cit) According to Wollaegar and Shands (loc cit) the thrill and the murmur may be heard anywhere over the dilated veins, but are better heard over the epigastric region In the first case of the present series a faint murmur was heard at the lower end of the dilated veins in addition to the harsh murmur in the epigastric region It was better heard in the recumbent rather than in the erect position Why the murmur is not present in every case of cirrhosis of the liver can be explained by the fact that the number of cases showing abnormally dilated and tortuous veins are few and only when blood passes from

the portal veins to these dilated veins can the murmur be produced. In one of the cases of cirrhosis of the liver with this abnormal venous dilatation, the murmur was carefully looked for and it could not be detected. The venous hum is heard also in the collateral circulation of thrombosis of the portal vein (Hatzieganu and Sharteu (loc cit)). The murmur is occasionally heard over the enlarged spleen (Kelly and Vincent Lyon (loc cit)). Catti (1907) and Thayer (1911) have observed the thrill and the murmur over the enlarged spleen in a larger number of cases (25 per cent). The murmur has been explained by Catti as the result of the kinking of the dilated splenic vein. We have not heard the murmur over the splenic area although it has been looked for on several occasions.

Cruveilhier-Baumgarten syndrome is diagnosed by the presence of abnormally dilated and tortuous veins over the epigastric region, and the systolic thrill and loud murmur over the dilated veins in the epigastric region or at the lower end of the sternum. In the foetus the umbilical vein carried blood from the placenta to the liver, and a few days after birth it becomes converted into the round ligament. In a few cases it remains patent for about 1½ inches from the junction of the portal vein, and this will be the first channel that will be utilised for the collateral circulation in cases of cirrhosis of the liver. The dilated vein might be the umbilical or para-umbilical vein, and this might be easily missed in the post mortem examination unless one carefully searches the falciform ligament. The blood in these veins runs from the umbilical vein to the veins of the anterior abdominal wall in a direction exactly the opposite of what occurs in foetal circulation.

SUMMARY

1 Two cases of Cruveilhier-Baumgarten syndrome are described. The characteristic signs are (a) abnormally dilated and tortuous veins in the epigastric region, (b) a prominent thrill and a loud venous murmur over the dilated veins, and (c) cirrhosis of the liver. In the second case ascites appeared only one year after the diagnosis of the syndrome.

2 The literature of the syndrome is reviewed.

Acknowledgements

Our thanks are due to Dr A. K. Narayana Menon for the biochemical investigations and to Dr C. Benjamin for the photographs.

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THE AURICULAR WAVE

AN EXHAUSTIVE INQUIRY INTO THE PHYSIOLOGICAL AND PATHOLOGICAL VARIATIONS OF THE P WAVE (OR AURICULAR WAVE) OF THE ELECTROCARDIOGRAM

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(Continued from page 10)

Criteria of "abnormal"—There is considerable confusion in the medical literature about the definition of an abnormal or pathological P Wave. Conflicting views have been expressed about the line of demarcation between the normal and the pathological P wave. For example, Katz regards a P wave as abnormal if it is higher than 3 mm in amplitude, broader than 0.12 sec or clearly notched. According to Pardee, a P wave is abnormal if it is over 2 mm in height, over 0.10 sec in duration and clearly notched. The existence of any two of these criteria is sufficient for regarding the P as abnormal. In a study of the P wave by White and Burwell in 1924, this wave was considered abnormal if its amplitude exceeded 1 mm in Lead I or 2 mm in Lead II or if the duration of P exceeded 0.1 sec in any lead. Alexander, Knight and White (1925), considered the P wave abnormal when its amplitude exceeded 1 mm in Lead I, or 3 mm in Lead II, or if its duration exceeded 0.1 sec in any lead.

From a study of our series of normals, it appears that a greater latitude may be allowed both in amplitude and duration of P wave before labelling it as abnormal. Even in perfectly normal records, P wave amplitudes of even 3, 2 mm and P wave duration as high as 0.15 sec were encountered several times.

Various abnormalities of the P Wave—Factors frequently concerned in alterations of P wave contour are —

(1) Alterations in the site of the pacemaker or impulse formation (2) alteration in the course or path of the excitation wave through the auricular musculature (3) alterations in mass or bulk of the auricular musculature (4) alterations in the lie or position of the heart

Abnormalities of the P wave, numerous as they are, can roughly be considered under the following headings —

- A Variations in the spacing of P waves
- B Cycle variations in contour of the P waves
- C Increased height or amplitude of P waves
- D Increased duration of P waves
- E Notching of P waves
- F Flattening or low amplitude of P waves and Inversion of P waves
- G Apparent and real absence of P waves
- H Replacement of P waves by other types of waves

A Variations in spacing of P Waves—The essential feature here is the irregularity or varying time relationship between successive P waves. There is a loss of rhythmicity as far as the P waves are concerned —

Sinus Arrhythmia—Where there is a gradual waxing and waning of the heart-rate, usually caused by alterations in the tone of the vagus nerve. There is a varying time-relationship between successive auricular deflections. Sinus arrhythmia has been classified by some authors into two main types viz—(1) The phasic form, where alterations in rate of the heart are in conformity with phases of respiration and (2) non-phasic form where no such association exists. The phasic form is said to be about 170 times as common as the non-phasic form (Katz)

The other classification of sinus arrhythmia is into (1) Physiological type or respiratory type, (2) Deglutitional type, (3) Post-digitalis type, to which may be added a fourth group, (4) The senile or arteriosclerotic type, such as has been described by Bellet and McMillan

According to Katz, information can be gained about the nature of sinus arrhythmia by attention to two factors viz the contour of the P wave and the duration of P-R

1 If the P wave contour and the duration of P-R are unchanging and then the S.A. is due to a simple "irregular discharge of a single pacemaker"

2 If the P wave contour changes but P-R remains fixed then the changes are probably due to the effect of respiratory movements on the position of the heart

3 If the P wave contour and P-R interval are both changing then there is a "wandering of the pacemaker within the sinus node" provided the P-R interval does not fall below 0.12 sec

It is to be noted that in the great majority of cases of sinus arrhythmia, the P waves remain constant in shape and size in spite of considerable alterations in rhythmicity, this is not surprising in view of the fact that in spite of fluctuations in the tone of the vagus nerve the spread of the contraction wave through the auricular musculature remains unaffected. In a small number of cases of sinus arrhythmia, however, the P waves do show variations in form and size, probably due to a shift in the pacemaker. The S.A. node is almost 3 to 5 cm in length and alterations in the tone of the vagus do tend to displace the site of impulse-formation within the node itself. It is said that increase of vagus activity displaces the site of impulse-formation downwards while decrease of vagus activity has the reverse effect. This phenomenon of a "shifting pacemaker" is encountered much more often in the non-respiratory than in the respiratory form of sinus arrhythmia

Sino-auricular Block—In this condition, complete beats are missed out, both auricular and ventricular waves being lost

The condition may be noted for a few cycles only or for even long periods of time. During the block, the intervals between the successive P waves are almost if not exactly double the normal P-P intervals.

The exact mechanism of sino-auricular block remains doubtful, it has been attributed to an increase in the tone of the vagus. In any case, this condition is perfectly benign with no evil import.

B P Wave Variations in Contour—Even in the same lead of an ECG the P waves may exhibit considerable latitude as regards contour or form. Such a phenomenon has been noted even in perfectly normal records.

Variations in the contour of P are attributable to the following main causes —

1 Alterations in the position or lie of the heart with respiration. This type which may be considered a normal variation, is undoubtedly the commonest type of all.

2 Alterations in the site of origin of the impulse or altered location of the pacemaker of the heart—the so-called “shifting or wandering pacemaker”.

The shift of the pacemaker may be (a) within the limits or confines of the sino-auricular node in which case the P-R interval does not fall below 0.12 or (b) the pacemaker may “wander between the S A and A V nodes”.

In this type the P wave undergoes changes in contour while the P-R interval varies enormously in duration (even going below 0.12 sec.) as a rule, bigger P waves occur during rapid phases and smaller and inverted P waves during the slow phases.

3 In rare cases, there is “electrical alternation of the P wave”. The P wave in this condition is alternately high and low.

During this course of infectious diseases, like pneumonia, bronchopneumonia, diphtheria and scarlet fever, variations in contour of the P wave are common enough to attract attention. These alterations of contour are, as a rule transient and disappear during convalescence or during fever itself, but at times they persist for a long time as one month or more after the termination of fever.

The P wave may become larger, smaller or wider than normal, it may become diphasic or inverted or may develop notching. These variations in contour have been attributed to (1) Toxic effects on the myocardium from absorption of “toxic by-products” (2) due to the associated pyrexia or hyperthermia (3) due to associated myocarditis, (4) due to effects on sympathetic or parasympathetic nerves.

P wave alterations are particularly frequent during the active phases of rheumatic fever and are quite unrelated to or independ-

ent of valvular defects They may arise long before any valvular lesion proper develops

5 P wave abnormalities are frequent, immediately after attacks of Coronary Thrombosis The P wave, in such cases, is usually longer than normal but may become smaller, or wider or diphasic or inverted or notched or may actually disappear

6 In Hyperthyroidism, P wave abnormalities are frequent As a matter of fact, Katz regards P wave changes as being commoner than T wave changes in cases of this sort Alterations in size and shape are common enough during the height of hyperthyroidism, but it is worthwhile remembering that some of these alterations of size or contour are reversible or remediable, and tend to disappear after subtotal thyroidectomy

C *Large P Waves or Increase in amplitude of P—Causation* — There is general agreement that large or "high voltage" P waves are usually secondary to hypertrophy of the auricular musculature This is based on concrete clinical evidence The association of large P waves with clinical conditions like mitral stenosis and cor pulmonale, both capable of giving auricular hypertrophy, is frequent enough to merit this conclusion

In the present state of our knowledge, it is not possible to say from study of an abnormally large P wave, which auricle is particularly or predominantly hypertrophied Left auricular and right auricular hypertrophy are electrocardiographically indistinguishable

Experimentally, Lewis has shown that artificial crushing of an auricular appendix in animals may lead to the appearance of a large P wave in the cardiogram These findings, based on one solitary instance, have not been substantiated by other workers

There are cases (e.g. in Coronary Thrombosis) where the cause of a large P wave remains obscure and undetermined The solution to this problem necessitates a proper correlation of clinical data and post-mortem findings

Is there a quantitative relationship between the amplitude of P and the degree of auricular hypertrophy? Goddard, after investigating this problem, has arrived at the conclusion that there is some sort of inconstant relationship between these 2 factors He regarded P wave as "large" when these waves were larger than the T waves in the same curve ($P-T=1+$) He found "large" P waves in 54 per cent of cases of mitral stenosis, also, 45 per cent of all examples of "large P" belonged to the category of mitral diseases Hence some relationship between the amplitude of P and auricular hypertrophy is obvious The relationship between these factors is not strictly quantitative because at post mortem slight auricular hypertrophy may be encountered in cases with huge P waves and severe hypertrophy in the presence of small P waves

Clinical states associated with large or "high" P waves

In a series of 132 cases with "abnormally high P waves" investigated by Alexander and others, the distribution of cases was as follows—55 per cent of the cases were definitely and another 5 per cent probably cases of mitral stenosis, 14 per cent were definitely and 2 per cent probably cases of congenital pulmonary stenosis, 2 per cent of the cases displayed interventricular defect while 14 per cent were cases of sino-auricular tachycardia without any evidence of co-existing mitral stenosis or congenital heart lesion, 8 per cent of cases were examples of high blood pressure

The most important causes of P wave enlargement may now be considered

There is no doubt that "stenosis of the mitral valve" constitutes by far the commonest and most important of all the causes of P wave enlargement. Considerable literature has accumulated on the subject of P wave abnormalities in mitral disease. Increase in height and duration of the P wave in cases of mitral stenosis, has been described by Einthoven (1906-1907), Kraus and Nicolai (1907), Samojloff (1909), Goddard (1915), Alexander, Knight and White (1925), Pardee (1933) and others

According to Frank Wilson, P waves in advanced mitral stenosis are frequently large, broad and display other peculiarities of configuration e.g. notching. Commenting on P wave abnormalities, Weiss makes the cryptic statement that "bifurcation and other abnormalities of the P wave are most often encountered in advanced mitral disease"

In a series of 57 cases of mitral stenosis with normal rhythm studied by White and Burwell (1924) as many as 44 cases or 77 per cent had abnormally high P waves in Lead I (over 1 mm high), in Lead II (over 2 mm high) or in Leads I and II

In a series of 58 cases of mitral stenosis with normal rhythm observed by Alexander and others, as many as 84 per cent of the cases displayed abnormally large P waves in either Lead I, Lead II or in Leads I and II. According to Alexander and others, the amplitude of P in Lead II exceeds 3 mm in 68 per cent of cases of mitral stenosis

According to Alexander, Knight and White the majority of papers dealing with the subject of P wave in mitral stenosis deal with the height or amplitude of the P wave rather than with the duration of this wave. This attitude they ascribe to the following 3 reasons: (i) The amplitude of a given wave is more evident and more easily measured than its duration (ii) The duration of P is difficult to measure on account of the auricular T wave (iii) The amplitude of P is more frequently affected in mitral stenosis than the duration of P. In their series of mitral stenosis, Alexander et al, could not find a single case of mitral stenosis with increased duration but normal amplitude of the P wave. The opposite finding i.e. increased amplitude with normal duration, was fairly common.

According to Pardee, the P wave of mitral stenosis displays 3 main forms of abnormality —(i) Excessive height (i.e. over 2 mm in the lead of largest measurement) At times, the height of P may reach or even exceed 5 mm Increased amplitude of P is found in 75 per cent of cases of mitral stenosis (ii) Excessive duration of P (over 0.10 sec), this is said to occur in 85 per cent of records (iii) Notching of P, said to occur in 60 per cent of records

In the opinion of Katz abnormal P waves in rheumatic mitral stenosis are sometimes premonitory evidence of auricular fibrillation In the so-called "pre-fibrillatory stage of mitral stenosis bizarre, broad, notched and tall P waves" are very significant specially when accompanied by multifocal auricular extrasystoles

The authors have studied personally the electro-cardiographic records of 50 cases of mitral stenosis and 43 cases of mitral regurgitation

They found an increased amplitude of P in 69 per cent of cases This is low when compared with the figures of White and Burwell (77 per cent of large P waves in 57 cases) and Alexander et al (84 per cent in a series of 58 cases) The number of "excessively tall" P waves was also much smaller (12 per cent) than that of Alexander et al (68 per cent) in a corresponding series

In this series, in mitral regurgitation abnormally large P waves were present only in 44 per cent of cases

Again, in our series whereas the duration of the P waves of mitral stenosis showed a definite increase over the Indian figures of "normal" worked out by one of us (R.J.V.) at a previous investigation, the mitral regurgitant group showed no such discrepancy, indeed, in all except Lead II, the "duration" values were higher for normal cases

(A more detailed analysis of the P wave abnormalities in valvular diseases of the heart has been reserved for the next issue of this journal)

Congenital Heart Disease, especially congenital pulmonary stenosis

Large P waves are common enough in congenital heart disease, according to White and Burwell (1924), but considering that the strain in mitral stenosis is also on the right side of the heart, P wave abnormalities are much less common in the former condition

In the series of cases of congenital pulmonary stenosis reported on by Alexander and others, abnormally large P waves were encountered in Lead I alone in 79 per cent, in Lead II alone in 84 per cent, in Leads I and II in 68 per cent and in Lead I or II in 100 per cent In the series of 20 cases of pulmonary stenosis reported by White and Burwell, all 20 displayed abnormally high P waves in Lead I, Lead II or in both Leads I and II

Chronic Cor pulmonale—In cardiac disorders secondary to lung disease, the P wave may show increased amplitude or other

abnormalities In Katz' opinion, "tall P waves" are frequently encountered in Leads II and III in cases of chronic cor pulmonale, they are however not "tall, broad and notched" at the same time, as in cases of mitral stenosis In the case of pulmonary embolism or infarction, P waves have been shown to alter considerably in size and shape during the recovery phase and even for as long as 2 years after the vascular accident

Sinus Tachycardia—According to Frank Willson, the P waves are often unusually high in cases of sinus tachycardia, the duration of P is however seldom affected while other peculiarities of form do not occur

Hyperthyroidism—In hyperthyroidism, Katz and others have described large P waves which may be also abnormal in other ways

Infections and toxæmias—The P wave may display abnormalities of size and even shape in a percentage of cases of this type In the course of rheumatic fever and subacute rheumatism of children abnormalities of P wave contour i.e. "peaking" of the P wave, have been described Ballet and McMillan have commented on the occasional occurrence of "large but not wide" P waves in the presence of toxæmias

In Coronary Thrombosis—Master and others have described unusually large P waves with or without other abnormalities in a fair percentage of cases of coronary thrombosis The cause of such alteration has not so far been adequately explained, it is possible that correlation with autopsy material may serve to explain such abnormalities in the near future

In cases of cardiac failure, a progressive increase in amplitude of the P wave may be observed during the phases of recovery e.g. after rest and digitalis

D Unduly "small" P Waves.—The amplitude of P wave is said to be pathologically "low" or unduly small when it is less than 0.5 mm according to Katz, and under 1.0 mm according to Pardee in all the three standard leads of the electrocardiogram From the points of view of both diagnosis and prognosis unduly small P wave carry much less significance than unduly large P waves

Abnormally small P waves may be encountered even in normal individuals under the following conditions —

(1) Small P waves may appear at the end of expiration, when there is excessive "slowing" of the heart-pace, and (ii) small P waves may appear during pressure over the carotid sinus on one or other side In either case, the lowering of P wave amplitude is ascribable to an increase in tone or over-stimulation of the vagus nerve which may perhaps shift the pacemaker from the upper extremity of the SA node to the lower (Belle and McMillan) According to Pardee, the P waves are unduly small in about 10 per cent of normal individuals Small P waves are frequently associated with the following

pathological conditions Their occurrence, however, is neither necessary nor diagnostic

In hypothyroidism or myxoedema

In vitamin B deficiency or cardiac beriberi

As a matter of fact, the P waves are unduly small or minute in the great majority of cases of cardiac beriberi that I have seen

In pericardial effusion

According to Bellet and McMillan, small P waves are observed in cases of auricular dilatation and in hypodynamic states of the auricle According to Pardee diffuse or generalized auricular disease is likely to give small amplitude P waves, while focal disease is more likely to give notching

As the result of digitalis therapy

According to Pardee, they may arise in states of mal-nutrition leading to functional disturbances of auricular muscle e.g. in coronary insufficiency

E Notching of the P Wave—According to Pardee, a "double-peaked" or notched P wave is often due to unequal hypertrophy of the two auricles, as the result of which development of electrical potential in the two auricles arises asynchronously

Physiological notching of the P wave is a well-recognized entity and may occur in perfectly normal hearts According to Bellet and McMillan, perfectly normal individuals may display notching of the P wave in Lead III and occasionally in Lead II or in Leads II and III but in the opinion of these authors notching of P in Lead I is practically invariably indicative of auricular muscle disease The results of my electrocardiographic studies are not in accordance with those of Bellet and McMillan, in a series of 200 normal electrocardiographic records, notching of P in Lead I was encountered by me in as many as 37 records i.e. in 18.5 per cent of records, in 2.5 per cent of normal records, notching of P was observed in all the three standard leads

Pathological notching of the P wave has been described in a variety of disorders, the most important being —

Mitral stenosis and other valvular disorders of the heart

In the acute myocardial involvement of rheumatic fever or subacute rheumatism

In 1928, McMillan and Cook reported the occurrence of notching or bifurcation of the P wave in about 50 per cent of a series of 43 cases of acute rheumatism investigated by him

In a much larger series of 200 cases of acute rheumatic fever and subacute rheumatism investigated by one of us (R.J.V.) in 1937 at the Liverpool Heart Hospital, notching of the P wave was observed in as many as 128 records (64 per cent) In as many as 17 records (8.5 per cent) the notching of P was noted in all the three standard leads There is no doubt that transitory and mild forms of myocardial lesions are extensively common in the acute stages of rheumatic infection

As a result of digitalis or quinidine therapy

In cases of hypertension with strain on the left ventricle Recently, Paul Wood and Selzer have directed attention to the frequent and clinically significant occurrence of abnormal P waves with notching in cases of hypertension with left ventricular strain

In syphilitic heart disease (Bellet and McMilan)

Due to intra-auricular block

The authors have studied the incidence of notching in cases of mitral stenosis and regurgitation and they find that whereas notching is present in 75 per cent of their cases of mitral stenosis in one or more of the standard limb leads it was only present in 60 per cent of cases of mitral regurgitation examined

F Inversion of the P Wave—The usual cause of P wave inversion is the adoption by the excitation wave of an anomalous or abnormal course through the auricular musculature, this is probably due to the excitation wave arising at an abnormal or new focus in the substance of the auricle

Apart from the "physiological form" of P wave inversion that may be observed in perfectly healthy individuals, the following types of inversion are encountered under pathological conditions

In *mirror image dextrocardia*, or in *situs inversus viscerum* where the heart is situated on the right side of the chest instead of the left, the electrocardiographic deflections are all directed downwards in Lead I The P wave in Lead I is therefore "inverted" from both in such individuals with dextrocardia

In *Auricular extrasystoles*—In the case of auricular extrasystoles, the impulse originates from an ectopic focus within the auricular musculature, away from the sino-auricular node The excitation wave, therefore, adopts an anomalous course through the auricular muscle and leads to alterations in P wave contour The main points of note in such a case are (i) The abnormal appearance of the P wave which is frequently inverted or diphasic, (ii) the P wave occurring prematurely or before its allotted time, (iii) a normal P-R interval, (iv) a normal or practically normal QRS complex following on the abnormal P wave Occasionally, the premature P wave of auricular extrasystole is not followed by a ventricular complex (the so-called Blocked auricular premature systole)

In *Auriculo-ventricular or atrioventricular nodal rhythm* (the so-called "A. V nodal rhythm")

In this condition, the A V node takes over the role of the pace-maker The P wave is inverted because the impulse arising anomalously in the A V node has to travel backwards towards the auricle, in a retrograde direction Two main forms of nodal rhythm are recognised, depending on the inter-relationship between the S A node and the A V node —(i) the slow form Where the A V node takes over (with its natural rate of rhythmicity of about 40 to 50 per

minute) the function of the pacemaker from the S A node, which is abnormally depressed, and (ii) The Rapid Form which is due to heightening of the rhythmicity of the A V node above the level of that of the S A node. The rate here is rapid.

The position of the inverted P wave in the cardiogram depends on the site of impulse-formation within the A V node, three main forms being recognised (i) Upper nodal rhythm. When the impulse originates in the upper portion or superior extremity of the A V node (at the caput, head or auricular end of the node), the impulse reaches the auricle before it does the ventricle. The inverted P wave, therefore, falls immediately before the QRS complex the P-R interval being shortened.

(ii) Lower nodal rhythm. When the impulse starts at the lower end or inferior extremity of the A V node (the tail or the ventricular end) the impulse reaches the ventricle before it does the auricle, the inverted P falls behind the QRS complex in this case, between it and the T wave.

(iii) Middle nodal rhythm.—When the impulse arises from the centre or mid-portion of the A V node, the auricle and ventricle beat simultaneously and the P wave gets buried within the QRS complex and may remain invisible.

In connection with ventricular extrasystoles—Ventricular extrasystolic impulses as a rule do not reach the auricles but when they do, an inverted P (retrograde P wave) is discernible about 0.2 sec after the onset of the ventricular extrasystole and a fair distance in front of the upright P wave of the next normal beat.

In Paroxysmal Auricular Tachycardia—A paroxysm of auricular tachycardia simply represents a rapid succession of extrasystoles of auricular origin. The P waves are abnormal in contour and frequently inverted or diphasic. In some cases the P wave fuses with the preceding T wave and renders the definition of the auricular complex extremely difficult.

G Absence of the P Wave—This is met with in the following important conditions.

Sino-auricular block or sino-auricular standstill—This condition is due to the S.A. node failing to emit one or more impulses at the usual time, as a result, there is a "missing out" of one or more complete beats from the electrocardiogram. (The auricular and ventricular deflections are both missing for one or more cycles.) We have learnt to recognize the following main types of sino-auricular block.

In type (i) the whole beat is missed occasionally and normal rhythm is restored after it.

In (ii) alternate beats are dropped out, as a result the condition is diagnosed as sino-auricular bradycardia, it is encountered in athletes.

(iii) a third type where complete beats are missed out for varying lengths of time, there being a total pause or "sinus standstill" of several beats

(iv) where during a long sinus pause, a new pacemaker (the A V node) takes over and produces one or more nodal beats

Intra-auricular block—This is a rare condition reported as arising in intoxication with quinidine. The P waves or auricular complexes are absent for several cycles at a time, though the ventricular complexes go on appearing as usual.

The condition is likely to be mistaken for "middle nodal rhythm" where the P wave is buried within the QRS complex. In the latter case however, there will be at least some abnormality or peak suggestive of an auricular wave within the confines of the QRS complex.

From such genuine absence of the auricular deflection or P wave one must distinguish the so-called "*apparent absence of P*". Here, the auricular deflection is present but missed on account of abnormal situation within the cycle or through mistaken identity. Examples of such "apparent absence of P" are furnished, amongst others, by the following important conditions:

1 In one variety of A V nodal rhythm, i.e., the so-called "middle nodal rhythm", the P wave appears absent because it coincides with the QRS complex, it lies buried within the QRS complex and is difficult of recognition. Careful study of such a QRS complex will usually reveal some notch, peak, indentation or other abnormality corresponding to the buried P wave. In middle nodal rhythm, there is simultaneous activation of the auricles and ventricles.

2 In simple sinus tachycardia, when the rate of the heart is very rapid, it is common to find the P wave "fused with" or even "preceding" the T wave of the previous cardiac cycle. In the event of the fusion of the P wave with the T wave of the preceding cycle, the combined wave may be mistaken for a large T wave while the P wave may be erroneously regarded as missing.

3 In partial (1st degree) "heart-block", the P-R interval may be sufficiently increased in length to make the P wave coincide with the T wave of the preceding cycle, in such cases, the P wave which is not obvious to the eye, may be erroneously interpreted as missing.

Auricular standstill—In this condition, which is occasionally observed during quinidine therapy or after carotid sinus pressure, the auricle stops beating and there is cardiac standstill for a few cycles. The ventricle ultimately escapes and carries on.

Middle nodal rhythm (already described)—Here the P wave lies buried within the QRS complex and may appear totally absent. There is, however, usually some peak or abnormality of the QRS which discloses the presence of the buried auricular wave. In middle nodal rhythm, there is simultaneous activation of auricles and ventricles.

Upper or lower nodal rhythm with retrograde block—In upper or lower nodal rhythm, the P wave is usually discernible as an inverted peak either immediately before or immediately after the QRS complex. In some cases, however, the auricular wave may be totally absent because of "retrograde block" from the A V node to the auricles. This has been ascribed to the property of "undirectional conduction" possessed by nodal tissue, impulses are transmitted in the direction of the ventricles with ease while they reach the auricles with difficulty.

H *Replacement of P by other waves*—This is observed in the following conditions —

In Auricular Fibrillation—In this condition, the normal regular auricular waves are replaced by much smaller oscillations or "f" waves which are not only rapid (arising 400 to 700 times per minute) but are markedly irregular in shape, size and timing. These oscillations may be visible in the whole record, in part of the record or not at all, in the latter case the record between ventricular complexes is a perfectly straight line.

In Auricular Flutter—In this condition, which is much less common than auricular fibrillation, the anomalous peaks or oscillations are much larger and more regular than those in auricular fibrillation. The oscillations in any given lead are exactly identical like "peas in a pod", they display perfect regularity of time and shape and occur about 220 to 370 times per minute. They may be absent or indistinct in Lead I of the cardiogram.

Impure Flutter—Here the oscillations are large and show a mild degree of irregularity only, they are more like the oscillations of flutter than those of fibrillation.

J *Other abnormalities associated with the P wave*

Pseudo-reciprocal rhythm—This is a condition of nodal escape or nodal rhythm where a nodal beat is followed by an upright and normal looking P wave of sinus origin, which in turn is followed by a normal ventricular beat.

Reciprocal rhythm (very rare)—Reciprocal rhythm is also a condition of nodal rhythm of an abnormal type. The nodal beats are followed by inverted retrograde P waves of an abnormal contour. Sometimes one of these P waves is followed by a delayed and abnormal ventricular beat which is abnormal because of "aberrant ventricular conduction". According to Katz, it consists of "a retrograde P wave from an impulse arising in the A V node, which are spreading through the auricles returns to the A V functional tissue and finding a path in it which is non-refractory re-enters this region again to stimulate the ventricles."

(to be continued)

STUDIES IN ANAEMIAS

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and

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This paper is a study of a series of 54 cases of anaemias admitted in the service of one of us (JCP) at the P G Singhanee Hindu Hospital during the years 1939 to 1942

Every case was studied intensively in the laboratory as follows

Examination of the blood—In addition to the routine cytology, this consisted of determining all the relative and absolute indices. The main purport of this, was to determine the "type" of anaemia, the criteria for this being the MCV (Mean Corpuscular Volume), the MCHC (Mean Corpuscular Haemoglobin Concentration), the V I, (Volume Index), and the S I. (Saturation Index). For the M. C. V 75 to 96 cu was considered the normal range (Napier) the corresponding figures for the V I. being 0.825 to 1.19 (Sokhey). For the MCHC and the S.I. the normal range was 28.17 to 38.0 per cent (Napier) and 0.86 to 7.175 (Sokhey) respectively. Any value for the MCV above 96 cu or for the V I above 1.19 suggested macrocytosis and the values below 75 cu for the MCV and below 0.825 for the V I microcytosis. Similarly, any value below 28.17 per cent for the MCHC or below 0.86 for S I suggested the existence of hypochromia. The Vanden Bergh reaction was indirect positive in 10 out of 37 cases of tropical macrocytic anaemia (T.M.A.). The red cell fragility test showed increased resistance in every case. The Kahn Flocculation test was positive in four cases only.

Examination of the gastric juice—This consisted of a preliminary gastric analysis of a Rehfuess oat-meal fractional method and in those cases that showed absence of free acid (as judged by the Toppfer reagent) repetition of the test with alcohol as the test meal (Minot and Castle) and histamine as the optimum stimulus. The result of this procedure showed that in four cases of microcytic hypochromic group there was a histamine-fast achlorhydria, and, when considered in conjunction with other data 7 out of the 37 cases of T.M.A. also showed a histamine-fast achlorhydria.

Examination of the faeces—This revealed the presence of ankylostome ova in 3 cases.

Examination of the bone marrow—This was done by the sternal puncture method and one thousand nucleated cells were differentiated. When the data so obtained was compared with available figures for the normal Indians (Napier) this procedure was found to be of great service. Its main utility was in the differentiation between the Pernicious Anaemia (P.A.) and T.M.A., and in the case of the latter especially in those cases which exhibited a histamine-fast achlorhydria. In P.A. we found a erythroblastic-megaloblastic reaction, but haemoglobinised megaloblast predominated, in the T.M.A. the reaction

A paper read at the 54th meeting of the C S Medical College and K. E. M. Hospital Staff Society, Bombay, on November 10, 1943, at 9.15 p.m. with Dr R. G. Dhavagude in the chair.

was again erythroblastic-megaloblastic, but the erythroblasts predominated and haemoglobinised megaloblasts were absent or few (Terminology of Donne, Cunningham, and Sabin)

Table I illustrates the frequency of the "type" of anaemia in this series

Table I

R B C Size	R B C. Hb Content	No of Cases
Normocytic	Orthochromio Hypochromio	4 3
Macrocytic	Orthochromio Hypochromio	31 9
Microcytic	Orthochromio Hypochromio	1 6

Table II

Type	Total Cases	Etiology
Normocytic	7	Ankylostomiasis 2
Macrocytic	40	P. A. 3 T. M. A. 37
Microcytic	7	Ankylostomiasis 1 Idiopathic hypochromic 4

Table II illustrates the utility of the laboratory study alone in the diagnosis of the etiology of the cases in this series

In this series of 54 cases, 35 were males and 19 females. Most of the cases of T.M.A. were between the age group of 20 to 40 years, while 18, 20, 22, and 56 years was the age of idiopathic hypochromic anaemia consisting of three females and one male. Symptoms present in this series were diarrhoea, continuous or intermittent—stomatitis and glossitis, low fever, vague abdominal disturbances, in the order of frequency, besides the usual symptoms referable to anaemia. In the majority of cases there was glossitis, spleen was palpable in seven cases, pellagrous dermatitis in two and oedema in two others. Koilonychia was noted in all cases of idiopathic hypochromic anaemia. Poor diet as such or inadequate intake due to diarrhoea or stomatitis seemed to be one of the important aetiological factors in the majority of the cases of macrocytic anaemia. Malaria seemed to be responsible in three and in two cases the symptoms dated from the last pregnancy. In the microcytic group ankylostoma duodenale was present in three cases, and bleeding piles in 4 cases. Kahn flocculation test was positive in four cases out of the whole lot.

All the patients after thorough investigation were given hydrochloric acid by mouth if they were suffering from achlorhydria or hypochlorhydria, otherwise an alkaline gentian mixture. All macrocytic anaemia cases were treated with liver extracts alone and microcytic anaemia cases with iron only.

All the work was carried out in the P. G. Singhane Hospital and wish to express our gratitude to Dr. R. Row, Hon. Director, Singhane Hospital for giving us all facilities and for the permission to publish this paper.

DISCUSSION

Dr. M. J. Shah stressed the importance of clinical and laboratory investigations in case of anaemia. The latter were however expensive and beyond the reach of patients in private practice and impractical. Dr. J. K. Mehta inquired the reason of including haemorrhagic maculae produced by menorrhagia and piles in the group of tropical macrocytic anaemias. He also inquired whether diarrhoea was the cause or the result of the anaemia.

Dr. N. K. Sahlar mentioned that in the experience of Wills the finding of megaloblast in the peripheral blood was diagnostic of pernicious anaemia. He also said that according to Wills a positive indirect Van den Bergh reaction and the presence of achlorhydria were also helpful for differentiation of P. A. and T. M. A.

Dr. V. N. Patwardhan asked whether dietary history and evidence of deficiency were obtained in the series. He also wanted to know whether desiccated stomach was used therapeutically and whether there were relapses in cases cured by the administration of crude liver extract when the diet was not subsequently corrected.

Dr R G Dhayagude inquired whether nervous symptoms were present in these cases. He observed that evidence of ankylostomiasis and P. A. in this series was comparatively small. He wanted to know from Dr Bhende whether there was a similarity between the blood picture of P. A. and Ankylostomiasis.

Dr Bhende, in reply to Dr M J Shah said that far from being considered impractical, full investigation in every case of anaemia was imperative for the proper diagnosis and the correct treatment. He pointed out that without laboratory aid a case of ankylostomiasis could never be detected nor could a distinction be made between P. A. and T. M. A.

To Dr Sahlar's query Dr Bhende replied that the occurrence of indirect positive Van den Bergh reaction and a histamine fast achlorhydria in T. M. A. did increase the diagnostic difficulties but a thorough investigation with proper assessment of all the data was the only solution. The presence of megaloblast in the peripheral blood as diagnostic of P. A. (as suggested by Wills according to Dr Sahlar) was to him not a point of much help. Megaloblast may not be present in the peripheral blood till the degree of anaemia was severe and secondly, the so-called megaloblast meant different kinds of cell to different observers. To him the presence of a haemoglobinised megaloblast in the peripheral blood smear if at all would alone be very presumptive of the presence of P. A.

To Dr Dhayagude's question Dr Bhende replied that the 3 cases of ankylostomiasis showed either a microcytic or normocytic type of anaemia.

In reply Dr J C Patel said that he could not say whether diarrhoea was the cause or the result of anaemia. His impression was that in some cases diarrhoea might be one of the aetiological factors and in others the consequence of prolonged deficiency of vitamin B complex. He added that the history of malaria was obtained in three and syphilis in four. Menorrhagia was evident in two cases of tropical macrocytic anaemia, being probably due to deficiency of vitamin B factors. He further added that there were few cases of pernicious anaemia because the family history and investigations such as examination of blood and gastric analysis of other members of the family and in follow up of these cases suggested that the majority of the macrocytic anaemias were cases of tropical macrocytic anaemia. In replying to Dr R G Dhayagude, he said that history of nervous symptoms were inquired into very carefully and only in 3 cases were they obtained. He added that there were only three cases of anaemia due to *Ankylostoma duodenale* and such a small number was probably due to a better class of people seeking admission to the Slaghnaee Hospital as compared to the K. E. M. Hospital. He observed that deicated stomach was not used in the treatment of these cases due to its prohibitive cost and inavailability of free samples. He concluded that errors in diet were causes of anaemia in some of the cases and the continuation of these errors resulted in some of them relapsing and necessitating readmission to the hospital.

In his concluding remarks Dr R G Dhayagude said that Drs Bhende and J C Patel had given an account of cases of anaemias as they ought to be studied and they had brought out very clearly the differences between tropical macrocytic anaemia and P. A. He observed that this differentiation was very necessary in the institution of rational therapy in anaemias. He congratulated the speakers on their excellent paper and expressed a hope that cases of anaemia admitted to the K. E. M. Hospital would be studied with the same scientific spirit with which they had been investigated and treated at the Singhanee Hospital.

Correspondence

Sir,

In the discussion on our paper entitled "Studies in Anaemias" (Y. M. Bhende & J. C. Patel) Dr N. K. Sahlar said that according to Wills one point of distinction between Pernicious Anaemia and Tropical Macrocytic Anaemia was the presence of Megaloblasts in the peripheral blood in Pernicious Anaemia. In reply to this I made it clear that we did not share this view. On referring to Wills' original papers I find that Dr Sahlar's statement is not borne out by the facts recorded in her communications. For instance Wills (1930) states "In T.M.A. nuclear forms of red cells do occur but are infrequent except in a few cases where there is a shower of normoblasts, true megaloblasts are found but normoblasts predominate." In another paper (Lucy Wills & Bilimoria 1932) she states, "In experimentally produced anaemias in monkeys megaloblasts were found at the height of anaemia but normoblasts were more frequent, the anaemia in this respect resembling T.M.A. rather than true P.A." Napier (1939) states, even more categorically, that he has never seen a typical haemoglobinised megaloblasts of P.A. in peripheral blood in a case of T.M.A. though occasionally he has seen a basophilic megaloblast that occurs in normal bone marrow. We readily subscribe to Napier's view.

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LAXATIVES AND PURGATIVES OR CATHARTICS

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It was suggested to me sometime ago that I should write something that might be of help to those beginning practice, on the uses of Purgatives. At that time I put away the suggestion and that for two reasons. First I thought the subject to be a very common place one. Everybody interested in medicine knows about purgatives! and secondly I wondered how it could be possible to write a short article on so wide a subject. Possibly neither of these reasons was a valid one. There may be young practitioners who are sometimes at a loss as to what to prescribe in a given case and even though the subject is too big for a single article, at least something can be said which may prove helpful. What then are Laxatives? Any preparations that have an aperient (Aperiens Opening) or mild purgative effect on the intestinal tract. They may act centrally, i.e., through the nervous system, systemically, i.e., only after absorption into the blood stream, directly, i.e., locally on the bowel, or even indirectly i.e. aiding or hindering the action of some other drug or secretion. Many food stuffs are mild laxatives, these act by increasing peristalsis by their bulk, their roughage, and the mineral salts which they contain. Many fruits are laxatives, i.e., Figs, Dates, Prunes. Syrup of Figs is a popular proprietary laxative, and the B.P.C. contains the preparations Syrupus Ficorum and Syrupus Ficorum Compositus. Both fresh and dried figs contain appreciable quantities of A and C vitamins also sugar 75 per cent, nitrogenous material 5 per cent, ash, i.e., mineral matter 2 per cent. Both figs and prunes are contained in confectio Sennae B.P. Dates and Prunes are similar in composition to Figs. Each of them being palatable, demulcent, and laxative they are of special value for the treatment of constipation in infants and young children.

Agar and Isafgul—Agar is a dried gelatinous substance, its laxative properties are chiefly due to the property it has of increasing its bulk in contact with water. Taken internally it forms a bulky stool and in this way promotes peristalsis. Agar is also an emulsifying agent and is therefore popular in such proprietary medicines as Agarol, Petrolagar, etc., laxative preparations combining Liquid Paraffin and Agar-agar. The B.P.C. contains no fewer than six emulsions of Agar and Liquid Paraffin, plain or in combination with other substances.

Ispaghula—Spogel seeds or Isafgul, are the mucilaginous seeds of *Plantago Ovata*. They too act by this property of forming a bulky mass in combination with water. They are soothing, demulcent, and laxative to the bowel, and were official in the B.P. 1914. (It is to be regretted that they have been deleted as they are inexpensive, keep well, and can be obtained anywhere in India as a bazaar medicine.)

The seeds of *Plantago Ovata* marketed as proprietary articles are much more expensive, but, apart from being cleaner and flavoured, are in no way superior to the country seeds. One such proprietary is "Siblin" P.D. & Co., and there was up to the war a continental packing.

The fixed oils of the B.P. are demulcent and mildly laxatives. They are —

Oleum	Amygdaloe
"	Arachis
"	Gossypii Seminis
"	Lini
"	Olivae
"	Sesami

whilst the most important of them all is *Oleum Ricini*

Castor Oil—is deservedly popular as a mild purgative because it combines with certain action. (It acts in from 2 to 8 hours) the property of being only slightly irritant and causing little hyperoemia. It can be used even where there is inflammation of the intestine, and is the least doubtful drug in conditions in which there may be a difference of opinion as to the expediency or propriety of purgatives. It is chemically an inert triglyceride of ricinoleic acid and only becomes aperient when it has been to some extent saponified in the intestine by the bile and the fat decomposing ferment of the pancreatic juice into glycerin and free acid. A part remains unsaponified and thus mechanically assists peristaltic action by lubricating the bowel and softening the scybala. Castor Oil has, therefore, a three fold action by virtue of the glycerin, the soap, (sodium ricinoleate) and the unsaponified oil. It is to be regretted that much of the castor oil used in India as a medicine is neither expressed in the cold (cold drawn) nor refined (tasteless castor oil) and for these reasons is nauseating and objectionable to sensitive patients. Its taste and smell are its chief drawbacks. It will be noticed that it begins to act high up in the small intestine, i.e., where the duodenal contents come into contact with bile and pancreatic secretion.

Paraffinum Liquidum—Liquid paraffin a laxative obtained from mineral sources, viz. liquid hydrocarbons obtained from petroleum. In this preparation we have possibly an example of a purely mechanical action. It adds something to the bulk of the faeces but it acts chiefly as a lubricant. Though a popular remedy for chronic constipation it has serious drawbacks which personally I consider outweigh its usefulness. In this connection let me quote you from an article which appeared in the *Journal of the American Medical Association*, 117, 1335, 1941. "On the harmful effects of liquid paraffin," The writer brings forward evidence against the use of this drug as a laxative. He points out—1. The rectum is not a reservoir. Functionally it is but a short passage to the exterior. The true reservoir is formed by the sigmoid and the descending and transverse colon. Faeces may remain in this portion of the bowel for sometime without ill effect.

Once the faeces enter the rectum, they should be evacuated with the establishment of the defaecation reflex. This initiates a strong peristaltic contraction of the colon, the contraction of its longitudinal fibres and the consequent shortening of the rectum by the levatores-ani, combined with the simultaneous onset of peristalsis, accompanied by a co-ordinate relaxation of the anal sphincters, resulting in the evacuation of the faeces. Failing this, as Alvarez, Hurst and others have pointed out, a person will have pressure symptoms of headache, foul breath, furred tongue, malaise and mental sluggishness. Liquid paraffin destroys this normal physiological process. The competence of the recto-sigmoid "valve" is destroyed and as a consequence the reservoir effect of the more proximal bowel is lost. Continual leakage from above results in the rectum being kept partially full most of the time and causes its conversion into an abnormal receptacle for faecal material. There is not sufficient pressure to initiate the defaecation reflex, but there is enough faecal material present to cause symptoms of irritation. (2) It can now be safely asserted that liquid paraffin because of its preferential solubility, interferes seriously with the utilization of carotene, and to a lesser extent with vitamin A concentrate as well as with the fat soluble D. It makes little difference whether the liquid paraffin is plain or one of the emulsified forms in which the liquid paraffin content is reduced. Curtis and Horton have shown that amounts of liquid paraffin as small as 15 to 30 cc. would still be able to remove all the carotene from a normal diet if the oil comes in intimate contact with food containing carotene. (3) Evidence is accumulating that liquid paraffin may be absorbed, producing pathological changes in the liver and other abdominal viscera. (4) It is true that liquid paraffin is a laxative, and it usually indicates soft or liquid stools, so that patients with rectal disease frequently take regular large doses several times daily. In the author's experience this often serves to aggravate the local lesions (a) by making a faecal reservoir of the rectum, and (b) by making complete evacuation impossible." I must leave it to my readers to weigh these arguments carefully.

Sulphur Proecipitatum—Milk of Sulphur. Sulphur sublimatum. Flowers of sulphur. The dose for each is the same (1 to 4g.) but it is the first named that is most often prescribed for internal use, and it is the milk of sulphur which is used in the preparation of *confectio sulphuris B.P.* In these days we are in danger of being entirely carried away from drugs which gave entire satisfaction to our forebears, this I think is rather a pity. In the March 4, 1944, *British Medical Journal* you will find an interesting paper on "Bacillary Dysentery", "A comparative study of treatments", and as you read it you may be surprised to find how closely the alkaline aperients and chalk approach in value to sulphaguanidine. This is an aside, but it bears out my contention, viz. that newer, more expensive, more difficult to obtain, and often much more toxic drugs should not in every case replace the older preparations. It may not be true that, 'the old is better', but it is sometimes worth considering that the old is nearly as good. To

return to our subject, sulphur is a pharmacologically inert substance. It does not act until it reaches the lower part of the small intestine where in the presence of excess of alkalis it is converted into sulphuretted hydrogen, (H_2S), which irritates the mucous membrane of the intestinal wall and causes increased peristalsis. The alkaline sulphides are themselves laxative in action, they are formed slowly as the H_2S is evolved gradually therefore the laxative effect of sulphur is slow, steady and prolonged. The hydrogen sulphide formed in the intestine is for the most part absorbed, oxidised in the blood, and excreted as sulphates. The part that escapes oxidation leaves the body through the skin and lungs, imparting to the sweat and breath its own unpleasant odour. This is the main objection to its use.

Bitters—The official bitters act by increasing gastric secretion thus they act by stimulating the appetite and improving digestion. In this way they are also mildly laxative. The bitters are usually divided into three classes, viz simple bitters, aromatic bitters, and astringent bitters. The last named contain tannin bodies and for this reason are not laxative. The simple official bitters are Gentian, Calumba, and Iuassia. Indian drugs that have like properties and may be used in their stead, are —Chirata (Indian Gentian) and Winter Cherry (Aswangandha). A non-official drug, (formerly official B.P. 1914), belonging to the aromatic bitters is Cascarilla Bark, Croton Eluteria, a native of the Bahama Islands. One would hardly prescribe a simple or aromatic bitter purely for a laxative effect, but it is well to remember this mild action so that they may be added to counteract astringent drugs such as Iron, and avoided when diarrhoea has to be controlled. They are all derived from vegetable sources and may be used in the form of Infusa, Tincturae, Extracta, Extracta Liquida, or Pilulae.

Sugary Substances—Liquorice, cassia fruit, tamarinds, malt and manna. Of these mannas and cassia are no longer official. Liquorice, the peeled root and peeled subterranean stem of *glycyrrhiza glabra*, consists of glycyrrhizin (a sweet, white crystalline powder, the calcium and potassium salts of glycyrrhizic acid) grape sugar, resin, starch and malic acid. It is the mildest of aperients and is used only for children. Recently a dispenser consulted me about a doctor's prescription, written "Rulv Glycyrrhiz". What he was intending, (as I found from him later), was *Pulvis Glycyrrhizae Compositus*, a compound powder, much stronger than simple *Pulvis Glycyrrhiza*, as it contains also, sulphur and senna. A simple rule to remember is that when the simple substance is meant the initial source should be first stated, i.e. *Radix Glycyrrhiza pulva* (There is no official *Pulvis Glycyrrhiza*), and *Rad Glycyrrh pulv*, and *Pulv Glycyrrh Co* are two entirely different substances as any dispenser understands.

Cassia Fruit—Cassia Fistula, a tree indigenous to India formerly official as *Cassiae Fructus*. If Indian doctors do not prescribe their own indigenous drugs, the B.P. authorities can hardly be blamed for removing them from the Pharmacopoeia. This is what has hap-

bened to quite a number of Indian preparations especially those that were contained in the Indian addendum of 1900) The pulp contains principally sugar, with small quantities of albuminoid matter and salts of calcium

Tamarindus—Tamarind, consists of the fruits of *Tamarindus indica*, freed from the brittle outer part of the pericarp and preserved with sugar It is contained in *Confectio Senna B.P* It contains the alcohol mannite (a sugar) and to this it owes its laxative properties Manna, though not official, is also a popular laxative for children, it may be eaten dry, or mixed with warm water or milk *Manna* is a dried sugary exudation from the European ash tree, *Fraxinus Ornus*

Malt.—*Extractum Malti* Extract of malt is prepared from sound malted grain of barley, *Hordeum distichon*, by digestion with water at a suitable temperature, not exceeding 55°C, until a viscous product is obtained It contains nitrogen equivalent to not less than 4.5 per cent W/W of protein Malt extract is a digested starch and contains chiefly maltose and dextrin Because of its sweet taste it is liked by children Its laxative action depends upon the inorganic salts it contains, and diastase an active ferment

Dose—4 to 16 mls Official preparations —

- 1 *Extractum Malti cum Oleo Monhuoe*
- 2 *Extractum Malti cum Olei Vitaminata A and D*

Magnesia—We have in the B.P a number of salts of magnesia, also several preparations in which one or other of these salts are contained

Official salts—*Magnesi Carbonas Levis*

- 2 *Magnesi Carbonas Ponderosus*
- 3 *Magnesi Oxidum Leve*
- 4 *Magnesi Oxidum Ponderosum*
- 5 *Magnesi Sulphas*
- 6 *Magnesi Trisilicatis*

Preparations from these salts —

- (a) *Pulvis Rhei Compositus* from both heavy and light carbonate of magnesia
- (b) *Mistura Magnesi Hydroxidi* from light oxide of magnesia and Sulphate of magnesia
- (c) *Mistura Senna Composita* from Sulphate of magnesia

Liquor Magnesi Bicarbonatis Syn Fluid magnesia is a solution of Magnesium Bicarbonate in water, saturated with Carbon Dioxide under a pressure of about three atmospheres It contains not less than 2.5 per cent W/v of $Mg(HCO_3)_2$ The first important point to remember in connection with the salts of magnesium is that the magnesium ion has very little effect when taken by the mouth, being very slowly absorbed and quickly eliminated The blood plasma contains 2 to 3 mgm of magnesium per 100 c.c., and the magnesium ion injected in combination with an acid radicle either subcutaneously or intravenously is a powerful nerve and muscle depressant but not a

laxative It is because magnesium salts are non-diffusible that they are in action purgative In the case of the oxides and carbonates of partly converted in the stomach into the chloride, and in the intestine, magnesia they both exercise a purgative action because they are by exchange with carbonates, into the soluble, not easily absorbed, bicarbonate It is a point worth noting that these salts, as also the *Liquor Magnesii Bicarbonatis* give a strong alkaline reaction to the evacuations "Why" asked a mother to me, "does my baby cry everytime she passes her motion and why is her back passage so red and sore?" I asked her about the laxative the child was getting, and she told me it was "Milk of Magnesia" Telling her to stop it at once, which she did, she was very surprised and very pleased that within a few days the soreness and the crying were both done away with

Magnesium sulphate belongs to a large class of substances known as saline purgatives — *Sodii et Potassii Tartras*, sodium phosphate, sodium sulphatepotassium acid tartras, *pulvis effervescens compositus*, carlsbad salt, and many mineral waters These all act as purgatives because the acid radicle contained in them is indiffusible, that is it is not absorbed (This has nothing to do with solubility in water) In the case of magnesium sulphate neither the base 'ion' nor the acid radicle ion are diffusible, but in cases where the base ion is absorbed (diffusible), i.e., potassium, and the radicle is not, the purgative action remains the same Sulphates, Tartrates and phosphates are especially indiffusible A 6 per cent solution of magnesium sulphate i.e. an isotonic solution will reach the large bowel in from two to three hours and 6 g will hold in isotonic equilibrium 100 c.c. of water, in this way causing purgation Thus salines act in the large intestine by osmosis, and this remains true even though the salt is in hypo-hyper, or isotonic strength

Glycerinum — Glycerin, a trihydric alcohol of the fatty series of organic substances obtained in the manufacture of soap Taken internally in small doses it has but little action as a laxative This is because it is readily absorbed and quickly and completely oxidised into C_2 and H_2O Large doses only taken by the mouth have a laxative effect It finds its chief use as a laxative when administered rectally (one or two teaspoonfuls) by means of a glycerine syringe Or it may be used in the form of a suppository *Suppositorium Glycerini* B.P.

We have completed what we have called the mild official laxatives of the *Pharmacopoeia* Purgatives or Cathartics are left over for a later paper Some Indian drugs closely allied to the official substances have been mentioned, as also several proprietary articles, which have quite unnecessarily taken the place of the official preparation for the same drug Readers will I hope be convinced that in the various standard books i.e., the B.P., the U.S.P. and the B.P.C. they will find all they need without going out of their way to add to the financial burden of their patients and to perpetuate what is more and more becoming a pernicious practice, viz the prescribing of patent and proprietary medicines

Original Contributions

BRONCHOSCOPY IN THE TREATMENT OF POST-LOBECTOMY ATELECTASIS

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The treatment of localised bronchiectasis has partly taken the form of lobectomy in suitable cases

The evolution of this operation has been slow since the excision of a diseased lobe may be accompanied by a number of complications. Originally the operation consisted of isolation of the affected lobe followed by securing of the lobe hilum by a snare or tourniquet. After most of the lobe had been cut away, what remained was secured by a series of mattress sutures and the chest drained by a water-seal system. There was inevitably some degree of sloughing of the lung stump with the formation of a bronchial fistula and consequent pleural infection, at the same time, collapse of the upper lobe was liable to add to the post-operative difficulties.

During the past 5 or 6 years, sub-total lobectomy provided by the snare technique, has given way to a total dissection lobectomy produced by isolation of the individual elements of the lung hilum, with the result that the formation of bronchial fistulae and pleural infection is less common. In other words it can be said that at the present time, the problem of pleural infection and fistula formation is well on the way to solution, there is still the problem of the ultimate fate of the remaining lobe to be considered.

Ordinarily this lobe, by compensatory emphysema, fills in the whole of that side of the chest, if, however, any obstruction of the upper lobe bronchus occurs, atelectasis will follow. Also if this lobe is not adherent it will drop to the bottom of the pleural cavity, from which position it is very slow to expand. This has led to the preliminary manufacture of pleural adhesions before undertaking the actual lobectomy, so that the upper lobe is maintained in its normal position and is capable of satisfactory function and downward expansion. This form of adhesion is usually effected by powdering the pleural surfaces with iodised talc or by the injection of strong silver nitrate solution, from the figures published by Sellors, Thomp-

son and Qvist it will be seen that the incidence of atelectasis was less when the upper lobe remained attached at the apex

In spite of this method to reduce the incidence of atelectasis with the subsequent danger of secondary infection in bronchiectasis, there are a number of cases in which the upper lobe, even though held in position, undergoes atelectasis. The onset of this phenomenon may be dramatic and should be recognised by sudden breathlessness, falling through of the mediastinum and above all by loss of movement on the affected side. Even after the operation of lobectomy, the chest on that side should move freely if not quite as well as on the opposite side, as soon as atelectasis occurs this movement is suddenly arrested, there is distress and the trachea when felt in the suprasternal notch is pulled towards that side.

The signs of the more dramatic types of lobar collapse do not require further description. A more dangerous type which may escape recognition, is one with an insidious onset. In these cases there are no sudden symptoms. Following operation, the air entry in the residual lobe should be reviewed at least once a day. Only by this means will any faint alteration in the character of the breath sounds be recognised. Paradoxical breathing is not a constant feature. A characteristic picture in a patient who has developed an insidious atelectasis overnight is—the respirations are slightly more laboured, there is pallor of the features, there are clinical signs of retained sputum in the bronchial tree. Attempts at making the patient cough only succeed in a superficial cough and clearing of the trachea with no improvement in the signs at the terminal bronchi. The pulse and temperature may not be raised. It should be emphasised that the above signs are indefinite and liable to be missed. The only certain means of establishing the diagnosis is by an X-ray, and this should be undertaken as a routine in every case. No reliance can be placed on physical signs and symptoms.

Various factors are at work in the production of post-lobectomy atelectasis. The problem of the individual characteristics of the patient should not be overlooked. It will be noticed that the reported cases consist of women and children. It is frequently possible to recognise the type of patient who is unlikely to cough and clear the bronchial tree in the vital first few days following operation. Such cases require the special attention of the nursing and medical staff.

Cases of bilateral bronchiectasis also require careful post-operative watching as the secretions of the active opposite lung may flood the relatively immobile operated side. As regards the technical aspects, an important point is the site of closure of the bronchus. If a long bronchial stump is left, it will collect a puddle of pus which will eventually overflow into either the dependent middle or lingula lobe bronchus. On the other hand, if the bronchus is closed too close to the upper lobe orifice, the post-operative oedema will close the upper lobe orifice and prevent adequate drainage.

Before Bronchoscopy

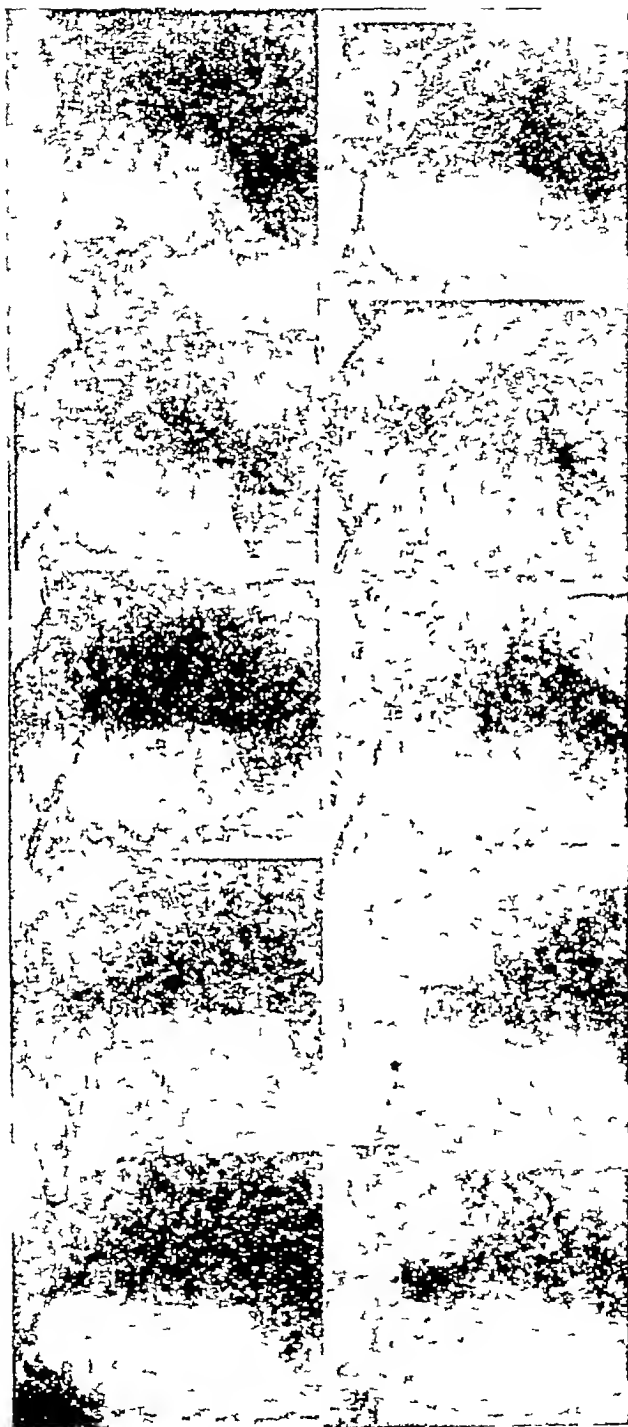
Case 1

Case 2

Case 3

Case 4

Case 5



Case 1

Case 2

Case 3

Case 4

Case 5

After Bronchoscopy

Figs. 1 to 10 Roentgenograms of the chests of cases 1 to 5 showing the collapsed lobes after operation before bronchoscopy in the upper figures and the re-expanded lobes in the lower figures after bronchoscopy

The prophylaxis of the condition is important. It has already been mentioned that certain types of patients require special care in the after treatment and should be encouraged to cough at frequent intervals. It is useless to leave the responsibility to a junior nurse. An experienced sister who will support a patient's chest and encourage him/her to cough, if necessary every half hour, is invaluable. In fact one can judge to some extent the standard of the post-operative thoracic surgical nursing by the incidence of atelectasis following lobectomy.

If at the operation there has been evidence of excessive bronchial secretion, an immediate post-operative bronchoscopy should be undertaken before the patient is returned to the ward.

In suspicious cases, prophylactic tipping is of value, although it should be abandoned after the fifth day unless the residual pleural space is dry.

The treatment of post-lobectomy atelectasis is well-established. On recognition of the condition, the patient should be made to undertake extra efforts at deep coughing, if necessary in conjunction with "tipping". If these measures do not succeed, bronchoscopy should follow without delay. Blind bronchial aspiration will undoubtedly relieve a number of cases but there is no doubt that full bronchoscopy is the only certain method of clearing the bronchial tree.

Technically, bronchoscopy is not difficult, in fact, these patients are unusually relaxed and accept the bronchoscope with moderate comfort. General anaesthesia is, of course, contra-indicated. I have, for other reasons, in a grave emergency, bronchoscoped a child of three years under local anaesthesia. In reasonably-minded children, local anaesthesia is quite sufficient preparation over the age of seven years.

Bronchoscopy performed in bed, or on very young children should not be undertaken by the inexperienced surgeon as grave, if not fatal, complications might result—extending from acute laryngeal oedema to rupture of the bronchial wall.

A characteristic picture is seen on bronchoscopy. As the carina is reached, a fair amount of frothy sputum requires aspiration. On entering the affected bronchus, a viscid blob of mucus can be seen blowing in and out of the upper lobe orifice. The latter is usually displaced from its normal position and points straight upwards. In fact, at times one can look straight down the lingula bronchus. When the initial mass of viscid mucus is sucked out, there is a flood of thinner secretion. The surgeon should not be satisfied with this and should encourage the patient to cough. He will be rewarded by the appearance of further reluctant, viscid masses of mucus which appear at the orifice and can only be aspirated with difficulty. Only when he is satisfied that both bronchial trees are completely dry, should the bronchoscope be withdrawn.

The following cases show the results of bronchoscopy in patients whose lobes did not re-expand following the usual conservative measures—

Case 1 E P Girl aged 12 Left lower lobectomy and lingulectomy for bronchiectasis (Mr Vernon Thompson). On the third post operative day and again on the 6th post-operative day showed collapse of remaining left upper lobe. On both occasions re-aeration of the lobe was effected by bronchoscopy.

Case 2 E R Woman aged 30 Left lower lobectomy (Mr Holmes Sellors) 24 hours after operation patient developed collapse of residual left upper lobe which was re-aerated following bronchoscopy.

Case 3 P H Woman aged 19 Bilateral bronchiectasis left lower lobectomy and lingulectomy (Mr V Thompson) Four days after operation, collapse of residual left upper lobe re-expanded after bronchoscopy.



FIG II—Roentgenogram of the chest of case 3, showing the left upper lobe which collapsed and never re-aerated following a left lower lobectomy. Bronchogram shows the development of gross bronchiectasis in the collapsed residual left upper lobe.

Case 4 A P Child aged 12 Left lower lobectomy for Bronchiectasis (B R B) Collapse of residual left upper lobe 48 hours after operation. Complete re-aeration after bronchoscopy.

Case 5 V I Woman aged 25 Case of bilateral bronchiectasis for which left lower lobectomy and lingulectomy were performed (Mr Vernon Thompson) Developed collapse of residual left upper lobe 48 hours after operation. Complete re-aeration after bronchoscopy.

Case 6 G C Aged 9 Two years ago she had a left lower lobectomy performed for bronchiectasis at an outside hospital. She developed collapse of the residual upper lobe which was treated conservatively and never re-aerated. Admitted to Harefield with persistent cough & sputum occasional staining. Bronchogram showed gross bronchiectasis in residual left upper lobe. Left upper lobectomy performed by Mr Holmes Sellors with uneventful recovery.

I wish to thank Mr T Holmes Sellors and Mr V C. Thompson for their permission to publish this paper. My thanks are also due to Dr K Stokes and Dr L G Blair for their permission to publish the case reports and x rays.

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TOXIC REACTIONS TO MASSIVE VITAMIN B₁ THERAPY

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Most monographs and papers on Vitamin B₁ are unanimous in their opinion on the point of tolerance to massive doses of vitamin B₁. According to them, vitamin B₁ may be given in heroic doses without fear of any untoward effects or toxic reactions, doses, several thousand times the average prophylactic requirement dose, have been tried, both in humans and in experimental animals, with no untoward effects whatsoever. There appears to be an exceptionally wide margin between the "therapeutic dose" and the "toxic dose" of vitamin B₁.

At the Roche Laboratories, New Jersey, as much as 500 mg of vitamin B₁ has been administered daily by mouth, for one month and "twenty times the usual intravenous dose" of vitamin B₁ given with no ill-effects whatsoever.

At the Abbott Laboratories, U.S.A., experiments on rats with intravenous injections of vitamin B₁ showed that 60 milligrams or 20,000 international units of B₁ per kilogram of body-weight could induce no visible symptoms of intoxication, this dose in human beings, corresponds roughly to about 4000 milligrams or 1,333,000 international units of vitamin B₁ for a man weighing 150 lbs. A dose twice this size, given intravenously in rats, caused a few fleeting nervous symptoms which vanished within a few minutes of the injection.

After an exhaustive series of experiments on animals, Molitor and Sampson (1930) have arrived at the conclusion that the therapeutic range of vitamin B₁ is so extraordinary that for practical purposes it is entirely non-toxic, the lethal dose is said to be from 25,000 to 50,000 times the daily normal requirement.

Clinically, doses of vitamin B₁ as high as 10 mg or 3333 international units have been given daily for long periods of time without any signs of intolerance (Vorhaus et al., 1935, Theobald, 1936). Weiss and Wilkins (1936) have administered as much B₁ as 130 mg or 40,000 international units daily with no toxic effects. It is because vitamin B₁ is not stored in the body that it can be given in such relatively massive doses with impunity.

However, in the medical literature of the past few years, there have been a few scattered references to the subject of vitamin B₁ intolerance or as one author puts it Hypervitaminosis B₁.

After an exhaustive enquiry into the toxic effects of symptoms of B₁ intolerance, reported in the literature of the past few years, it is possible to divide these cases into three main groups —

- (1) Symptoms of vitamin deficiency, usually of the nature of pellagra or ariboflavinosis as reported by Lehman & Nielsen

(1939), Salvesen (1940) and Braendstrup (1940), and attributable to a "fractional overloading" or overdosage of vitamin B₁

- (2) Sensitization syndromes or symptoms, as reported by Laws (1941), Schiff (1941) and Mills (1941) and due either to the vitamin itself or to the preservative employed in the preparation of the B₁ solution
- (3) Toxic symptoms of uncertain or vague aetiology, as reported by Steinberg (1938) and Leitner (1943)

In the first and largest group, are included cases where the toxic symptoms observed after massive B₁ therapy, are attributable to "an imbalance of Vitamin B factors" or to a "certain antagonism between the various components or factors of the B complex"

Lehman & Nielsen (1939), Salvesen (1940) and Braendstrup (1940) have all called attention to the development of symptoms and signs of pellagra in patients treated with massive doses of B₁. In Braendstrup's case, a chronic dyspeptic, signs of pellagra were noted after the administration of as much as 220,000 international units of vitamin B₁ in three weeks

Recent experiments on rats at the Rowett Research Institute, Aberdeen, by Richards, have proved conclusively that "overloading with one component (of the B complex) e.g. B₁ can induce a definite deficiency of another component e.g. B₆". Symptoms of pyridoxine deficiency were reported in laboratory rats after excess doses of vitamin B₁

Paradoxically enough, massive doses of B₁ (upto 1 gram per Kg of body weight) have been reported by Bullard and Grundland (1940) to cause a "beri-beri-like syndrome" in pigeons

No suitable explanation has, as yet, been offered to explain the development of deficiency syndromes in cases treated on massive doses of B₁. According to one school of thought, the deficiency is "multiple" or complex to begin with and successful medication of the more apparent or preponderant deficiency (viz B₁) tends to bring out or show up the associated "component deficiencies", which were previously "masked" or "latent". In the words of Minot (1938), "nutritional failure in practice is seldom complete or simple. It is often complicated by a variety of mechanisms inducing its origin or aggravating the initial abnormality"

According to Sydenstricker (1939), "nutritional disturbances in the human subject are always complex" and "it is most important to realize that few patients suffer from a single avitaminosis". Other clinicians, prominent in the field of nutrition, have also emphasized this "complexity" of the "nutritional failure syndrome"

Though the above mentioned reports stress the frequency of development of symptoms of deficiency of one vitamin B factor by excessive dosing with another, there are also reports to the contrary. Unna and Clark (1942) observed no adverse effects in rats treated with massive doses of individual vitamin fractions while Klopp, Abels & Rhoads (1943) failed to induce any form of deficiency

ciency in humans after massive doses of vitamin B₁ administered for long periods of time

In 1941, several reports appeared in the literature on the subject of "sensitization to B₁" or to thiamine hydrochloride

In Laws' case of B₁ sensitization (1941), minor symptoms, like violent sneezing and pruritus, were noted after initial subcutaneous injections of B₁. Subsequent injections gave violent anaphylactic reactions, like oedema of the lips and eyes, massive urticarial wheals, tightness in the chest, dyspnoea and cyanosis with audible wheezing of the chest, all relieved by the administration of adrenalin.

Schliff (1941) reported a severe state of shock with profuse perspiration, nausea and vomiting, involuntary voiding of excreta, collapse of the pulse, inaudibility of heart-sounds and blood-pressure sounds and cessation of respiration within a minute or two of an intra-gluteal injection of vitamin B₁. The patient responded to artificial respiration and injections of caffeine-sodium benzoate and adrenalin. This state of shock was attributed to "a possible sensitivity to Thiamin solution" which might have been injected by mistake into a blood-vessel.

In the case of Mills (1941), sensitization symptoms were noted after the oral administration of B₁.

Such sensitization syndromes after B₁ may be due, either to the Thiamin itself (in which case, it can be reproduced by the experimental injection of a specially prepared aqueous solution of chemically pure B₁) or to the preservative added to the B₁ solution (as in the case, reported by Jolliffe in 1941).

Toxic symptoms of uncertain aetiology have also been reported after vitamin B₁ therapy.

Steinberg (1938), while treating cases of chronic arthritis with massive doses of vitamin B₁, noted the development in some of the cases, of typical lesions of Herpes Zoster and involuntary muscle spasms, these symptoms disappeared on discontinuing B₁ therapy.

In 1943, Leitner reported two cases of prolonged vitamin B₁ therapy where toxic symptoms of an unusual nature were observed, in one of his cases symptoms of hyperthyroidism (headache, insomnia and palpitation) were attributable to the B₁ therapy.

In the light of the above observations, the following two case-reports are likely to prove of interest —

CASE I

A Parsee clerk, aged 45 was examined by me, in consultation in February 1945 for the following symptoms: general debility, loss of appetite and weight, indigestion and acid taste in the mouth.

On examination the cardiovascular and respiratory systems were found to be normal. The patient's conjunctivae were injected, the tongue had a glossy and polished appearance (more so in the centre of the tongue) with no fissuring along the edges while the angles of the mouth displayed definite fissuring (angular cheilosis). In the region of the elbows and extending for about 3 or 4 inches along the backs of both forearms were seen patches of dry and scaly skin with bluish pigmentation. According to the patient, all these features were of recent origin and were definitely noticed after he had been subjected to daily 100 mg. B₁ injections by his family doctor. This fact was confirmed not only by the patient's relations but also by the family doctor who admitted having given about twenty injections of B₁ during which course the scaly patches on the elbows and the oral lesions became increasingly apparent.

The patient was put on two Nicotinamide tablets (50 mg. each) three times a day (giving a daily dose of 300 mg. of nicotinic acid amide). In early April he was subjectively much improved, the indigestion had disappeared, his appetite had definitely returned and the skin lesions had

disappeared almost completely but for some tiny areas of brownish discoloration in the region of the elbows. The oral lesions were definitely better. The Nicotinamide treatment was now stopped and he was put on Riboflavin capsules (vitamin B₂ or G), 10 mg daily. At the end of May when re-examined, the patient was found to have made a complete recovery with no signs of glossitis or cheilosis whatsoever.

This case report illustrates how vitamin B in large doses may actually induce or aggravate allied vitamin B complex deficiencies.

CASE II

An obese Parsee woman, diabetic was under treatment with Insulin for her diabetic condition. She was getting daily morning injections of 40 units of protamine zinc insulin (Lilly). In view of some neuritic pains in the left arm and leg it was decided to give her vitamin B₁ parenterally.

After the very first injection of vitamin B₁, 50 mg given on the outer side of one thigh she developed a violent reaction within less than a minute. After complaining of a severe nausea and a sense of collapse she began to vomit out large quantities of undigested food and later bilious and watery fluid. She became deathly pale with slight cyanosis of the nails and profuse perspiration. The pulse which was rapid to begin with became practically imperceptible in a couple of minutes, muscle spasms were noticed in both lower extremities and the patient's consciousness was perceptibly "dulled" or "clouded". The breathing was extremely slow and periodic with long phases of apnoea. She was given 2 cc of Cardiazol-Ephedrin (Knoll) intramuscularly, in addition to being kept warm with blankets and hot water bottles. Within ten minutes there was considerable improvement in her condition and in another thirty minutes she was perfectly normal. In view of the early onset of symptoms after intramuscular injection of B₁ it is possible that the preparation might have been inadvertently injected into a vein or capillary and caused sensitization symptoms.

SUMMARY

The present case reports and discussion serve to focus our attention to three unusual aspects of vitamin B₁ therapy, viz,

- (1) Large doses of vitamin B₁, when administered, singly, for long periods of time, may bring about or accentuate symptoms of allied vitamin deficiencies. In case I, reported here, symptoms and signs suggestive of pellagra and ariboflavinosis, were noted after massive doses of B₁.
- (2) The advisability is emphasized of joint administration of the other fractions of the vitamin B complex, when contemplating massive vitamin B₁ therapy. The joint administration of some suitable oral preparation of the vitamin B complex may serve to prevent or offset the unpleasant side-effects of vitamin B₁ therapy.
- (3) Vitamin B₁, even in small doses, may occasionally bring about, in sensitive individuals, violent symptoms of shock with nausea, vomiting and peripheral failure.

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Critical Notes and Abstracts

DIABETIC NEURITIS A TENTATIVE WORKING CLASSIFICATION

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That the topic of diabetic neuritis is not a simple one is familiar to both internists and neurologists. The very term "diabetic neuritis" is in many cases a misnomer. In many of the cases in which the condition is called "diabetic neuritis", the main etiologic factor is not diabetes *per se*, in other cases the condition is not truly neuritis. Pain occurring in a patient with diabetes frequently has been all that was necessary for a diagnosis of diabetic neuritis to be made; consequently there has been a tendency for many essentially different processes to be referred to loosely by the term, "diabetic neuritis". Therefore, it seemed necessary to begin where I suppose I should logically have ended, namely, with a classification of diabetic neuritis. This is being presented as a hypothesis, in the literal sense of the term, that is, a tentative supposition or assumption as a basis of reasoning. It is not meant to be original, since it is really a synthesis of material derived from the literature as influenced by a recent study of several cases of diabetic neuritis.

Table 1 Classification of diabetic neuritis

-
- Group 1 Diabetes with pain**
- 1 Aching pains with cramps and tenderness.
 - 2 Legs affected especially, but diffuse pain may involve arms and back.
 - 3 Pain worse at night.
 - 4 No definite objective neurologic signs, other than tenderness.
 - 5 Diabetes out of control.
 - 6 Prompt relief with control of diabetes.
- Group 2 Ischemic neuropathy**
- 1 Definite evidence of obliterating arteriosclerosis almost always present.
 - 2 Insidious onset, patient more than 40 years of age.
 - 3 Incidence greater among men than women (2:1) but very rare in non-diabetic women.
 - 4 Main symptoms are pain, paresthesia, and cramps, especially at night.
 - 5 Involvement primarily of legs with progressive increase in involvement peripherally.
 - 6 Most frequent objective sign is areflexia.
 - 7 Course usually progressive.
 - 8 Occasionally considerable improvement after many months if vascular status of extremity improves.
- Group 3 Diabetic polyneuritis**
- 1 Peripheral polyneuritis and polyradiculitis with its secondary cord changes (neuronitis) also probably diabetic pseudotubercles included here.
 - 2 Relatively acute onset, may occur in young diabetic patients.
 - 3 Symptoms of neuritis represent a chief complaint.
 - 4 At height of process, degree of discomfort and disability frequently severe.
 - 5 Definite neurologic pattern: roots, peripheral nerves and so forth; objective neurologic signs are definite; process is frequently diffuse though legs are predominantly involved.
 - 6 Protein in spinal fluid increased in about 50 per cent of cases.
 - 7 Improvement in weeks to months.
- Group 4 Diabetic visceral neuritis**
- 1 Burning paresthesia of feet.
 - 2 No objective neurologic signs.
 - 3 Objective vasomotor changes.
-

Diabetic neuritis has been divided into four groups, as follows: group 1, diabetes with pain, group 2, ischemic neuropathy and group 3, diabetic polyneuritis, to these three usually accepted groups, I am adding a fourth group, diabetic visceral neuritis. Table 1 presents in summary fashion the distinguishing characteristics of each of these groups.

Group 1 is referred to with the noncommittal term, "diabetes with pain" The outstanding characteristics of this group are as listed in Table 1 The main complaints are aching pain with cramps and tenderness Although the legs are affected, especially, the discomfort may be diffuse and involve the arms and back. It is worse at night No objective neurologic signs other than tenderness are present The key to this group lies in the next two points, the diabetes is invariably out of control, and there is almost always prompt relief with control of the diabetes

In group 2, ischemic neuropathy, vascular sclerosis with arterial insufficiency of some degree is almost invariably present In this group, the onset is usually insidious and the symptoms go hand in hand with the signs and symptoms of the associated and causative obliterating arteriosclerosis Men are affected more frequently than women

TABLE 2 Classifications of diabetic neuritis used by various authors as they correspond more or less to the four proposed groups

Author	Group 1 Diabetes with pain	Group 2 Ischemic neuropathy	Group 3 Diabetic polyneuritis
Woltman and Wilder (1929)		8 cases	2 cases diabetic pseudotabes
Root and Rogers (1930)	Abnormal nutrition	Neuritis with deficient blood supply	Diabetic neuritis with paralysis
Jordan (1936)	Hyperglycemic type	Degenerative (and circulatory) type of neuropathy	Diabetic neuritis diabetic tabes neuritic type
Swartz (1940)	Diabetic neuritis group 1, without signs (Besides corresponding to my groups 1 and 2 this group probably also would include some of the cases which I am classifying in my groups 3 and 4)		Diabetic neuritis group 2 with signs

Pain, paresthesia and cramps, occurring especially at night, constitute the main symptoms of ischemic neuropathy Involvement is primarily in the legs with progressive increase in involvement peripherally The most consistent objective sign is areflexia Although the course is frequently progressive, occasionally, there will be considerable improvement after many months if the vascular status of the extremity can be improved

Next is group 3, diabetic polyneuritis Here are included peripheral polyneuritis and polyradiculitis, with its secondary changes in the spinal cord The clinical picture may be that of neuronitis and suggests the Guillain-Barre syndrome Whereas diabetic pseudotabes presents a more or less unique clinical syndrome, it may be dependent on changes in the peripheral nerves and roots, hence its inclusion in this group may be justified In diabetic polyneuritis, there is usually a relatively acute onset It may occur in the young as well as in the older diabetic patient The neuritis usually represents a chief complaint At the height of the process, the

degree of discomfort and disability is frequently severe. The diagnosis would be readily acceptable to a neurologist because the symptoms and signs present usually follow a consistent neurologic pattern, with particular involvement of the somatic fibres of the peripheral nerves or roots. Definite objective signs are demonstrable, the process is frequently diffuse. The protein of the spinal fluid is elevated in about 50 per cent of the cases. With usual diabetic control and with whatever supportive measures seem indicated, definite improvement usually occurs in weeks to months. Therefore from the prognostic standpoint, in spite of the frequent acuteness and severity of the polyneuritis, the condition may be thought of as being relatively "benign".

For the *fourth group* the term "diabetic visceral neuritis" is offered with apology. By it, I refer to involvement of the peripheral visceral motor fibres (that is the vasomotor fibres of the autonomic nervous system) and the corresponding peripheral visceral sensory fibres. This is offered as a separate group to stress the fact that involvement of these visceral fibres has escaped emphasis, although this may occur along with more or less involvement of the somatic fibres of the peripheral nerves. Evidence is being accumulated by Roth and Rynearson to show that in some cases of diabetic polyneuritis, striking vasomotor changes, suggestive of involvement of the sympathetic fibres, frequently are present. The picture of a peripheral visceral neuritis without associated involvement of the somatic components consists of burning paresthesia of the feet in the absence of objective neurologic signs and in the presence of objective vasomotor changes as would occur after sympathectomy. Such a picture has been observed in pellagrins.

Some of the workers who, in recent years, have made outstanding contributions to the subject of diabetic neuritis are given in Table 2. It was largely their factual material and classifications that were synthesized and correlated in evolving the classification presented herein, and this table shows where their types would fit more or less in this classification.

Woltman and Wilder (Woltman, H.W. and Wilder, R.M. Diabetes mellitus: pathologic changes in the spinal cord and peripheral nerves. *Arch Int Med* 44: 576-603 (Oct.) 1929) studied ten cases of diabetic neuritis and found arteriosclerosis of the nutrient vessels of the nerves present in all ten cases. This is not surprising, however, when their material is reviewed. In six cases, examination of the nerves was made in an extremity amputated for arteriosclerotic gangrene. The other four cases were necropsy cases in which the age of the patients at death ranged from forty-nine to seventy-five years. In eight of the cases clinically the picture was similar to the group called "ischemic neuropathy", two of the cases represented diabetic pseudotabes.

Root and Rogers (Root, H.F. and Rogers, M.H. Diabetic neuritis with paralysis. *New England J Med* 202: 1049-1053 (May 29) 1930)

discussed the causes of pain in the legs in diabetes under four groups, the three listed fitted more or less into the scheme as placed in Table 2 and a fourth called "pressure with referred pain." By this latter, they referred to pain from associated arthritis in diabetic patients causing pressure on susceptible nerves or pressure such as that causing peroneal palsy, or crossed leg paralysis, which Woltman (Woltman, H W Crossing the legs as a factor in the production of peroneal palsy J.A.M.A. 93 670-672 (Aug 31) 1929) has shown occurs with greater frequency in diabetic patients than in nondiabetic persons

Jordan, (Jordan, W.R. Neuritic manifestations in diabetes mellitus Arch Int Med 57 307-366 (Feb) 1936) in discussing neuritic manifestations in diabetes mellitus, reviewed 286 cases. He divided the cases into four types (Table 2) and then included the circulatory type with degenerative since they resembled each other in all essential features. Concerning his hyperglycemic type, Jordan pointed out that of thirty-four patients, ten showed dehydration, nine, acidosis and twenty-two neither. Therefore, neither dehydration nor acidosis was considered essential etiologically. Jordan admitted that he could not conclude that hyperglycemia alone caused the symptoms, since hyperglycemia is often present in diabetic persons without symptoms, yet it was the only factor present in all cases and correction of it was followed immediately by disappearance of neuritic symptoms. For this reason, he named the group the "hyperglycemic type." The hyperglycemia is evidence that the diabetes is out of control, probably at the present time no more than this can be said as to the cause of the pain in these cases.

In the series of Root and Rogers and in the series of Jordan, the essential characteristics of their respective groups are much the same as those of corresponding groups under which I have them classified in Table 2. This is necessarily so since this classification was moulded to a large extent, as already mentioned by extracting, organizing and correlating their material.

Jordan pointed out that there is a natural overlapping of the groups since the apparent important factors, hyperglycemia and arteriosclerosis which operate respectively in the first two groups, also operate at times along with other possible factors in the neuritic group. Thus the neurologic process as observed in the individual diabetic patient may well fall into two or more of the groups. For example, it is not uncommon to have diabetic polyneuritis affect a person who has occlusive arterial disease and some degree of ischemic neuropathy.

Swartz (Swartz, F.C. Diabetic neuritis Thesis, Mayo Foundation, 1940) in 1940, divided diabetic neuritis into two groups: group 1, without signs, and group 2, with signs. It is interesting that the most common symptom in his group 1 was paresthesia and in his group 2, pain. In his group 1, men outnumbered women 21, the sex incidence was about equal in his group 2. In twenty-four out of forty-one cases in his group 2 protein in the spinal fluid was increas-

ed Cases of Swartz's group 2 appear similar to the more severe cases of my group 3, diabetic polyneuritis, some cases of his group 1 would probably also correspond with the milder cases of my group 3, whereas others of his group 1 would probably correspond with one more of the other three groups

From the foregoing discussion it is clear that the sharp lines that have been drawn in the proposed classification are largely artificial. When its limitations are understood, however, it serves the essential purpose of a working classification.

Three representative cases illustrating all of the groups will be reported.

Case 1, illustrative of group 1 diabetes with pain.—The patient is a white man forty-eight years old, whose diabetes was discovered on his examination at the Clinic. His main complaints on admission were indigestion and right upper abdominal distress. He also stated that for two or three years he had noted the triad of symptoms of polyuria with nocturia, polydipsia and polyphagia with loss of weight. For about two years he had had burning numb feelings and aching pains in his legs and feet. These were present most of the time, were not aggravated by walking but were worse when he was tired and at night. Cool water seemed to give some relief.

On physical examination the pulsations in the dorsalis pedis and posterior tibial arteries were normal, the knee jerks and ankle jerks were normal. Vibration and position sense in the lower extremities were preserved. The concentration of blood sugar was 313 mg per 100 cc and there was a 7 per cent concentration of glucose in the urine. No acetone or diacetic acid was present in the urine. Roentgenograms revealed a non functioning gallbladder, which it was felt accounted for this patient's gastro-intestinal complaints.

Use of a quantitative diabetic diet and insulin was begun. Within a week the glycosuria was well controlled on a single morning dose of 20 units of protamine zinc insulin and 48 units of regular insulin.

The patient stated that two days after he was started on his diet and insulin there was noticeable improvement in the numb feeling and aching pains in his legs such that he felt better than he had felt in the previous two years. By the end of a week when his diabetes was well controlled, the pains and paresthesia had almost completely cleared.

Diabetic patients complain frequently enough of aching pains and cramps when their vascular and neurologic examinations are essentially negative that the clinicians seeing these patients have come to withhold judgment until the glycosuria has been controlled.

Case 2, illustrative of group 2, ischemic neuropathy. The patient was a white woman, fifty-nine years of age with diabetes, grade 1 to 4 (on a grading basis of 1 to 4 in which 1 designates the mildest and 4 the most severe condition) of twenty-one years duration. She started taking insulin about one and a half years before admission to the Clinic and was regulated on 10 units of protamine zinc insulin every morning.

The patient stated that among her other complaints of pruritus vulvae, blurring of vision, abscess of the buttocks and so forth, two or three years before admission she had had a gradual onset of pain in the feet with paresthesia which had become progressively worse. At first, she had rather typical pain of intermittent claudication, but in the year before admission, her feet had become so painful in the arch and heel that she was unable to walk enough to get claudication. Painful cramps and burning numbness kept her awake at night.

On examination the knee jerks and ankle jerks were found to be absent. There was slightly diminished sensation in the left foot and there was painful hyperesthesia of both feet. The pulsations were normal in the femoral arteries, diminished in the popliteal arteries and absent in the dorsalis pedis and posterior tibial arteries. Other evidence of arterial insufficiency was definite pallor on elevation of the feet for two minutes, definite rubor on dependency, a venous filling time of ten seconds in the right foot and of thirty seconds in the left, and a delay in return of color of ten seconds in the right foot and of thirty seconds in the left. Roentgenograms of the left leg revealed marked osteoporosis of the bones of the left foot and leg with calcification of the vessels. The patient was treated on a Sanders bed and with the usual routine for arterial insufficiency of the lower extremities. A slight improvement was seen after several weeks.

Case 3 illustrative of group 3, diabetic polyneuritis.—The patient was a white man, thirty-four years of age with diabetes mellitus grade 4 of seven years duration. He complained of weakness, loss of weight, generalized abdominal pain without relation to food, which was dull and constant but in addition had many characteristics of root pain; pain in the legs of sciatic distribution and of shooting character and cramping pain in the calves at night. He stated that the onset had been fairly definite and has occurred about six months before admission.

At the time of admission the diabetes was kept under control with a single dose of 26 units of protamine and 50 units of regular insulin every morning. Roentgenograms of the stomach and colon, an excretory urogram and a retrograde urogram were made because of the abdominal pain, all were negative. The pulsations in the vessels of the extremities were all normal. The patient had chronic rheumatoid spondylitis and moderate urinary insufficiency on the basis of pyelonephritis, but it was felt by the special consultants that the neuritic process was unrelated to these conditions.

The results of the neurologic examination may be summarized briefly as follows: The deep reflexes in the arms were markedly diminished, those in the legs were absent. In the sensory examination appreciation of pain, touch, vibration and joint sense were moderately diminished with a progressive increase peripherally in the arms and legs. There was definite muscular weakness which involved especially the dorsiflexor muscles of the feet and the muscles of the wrists and the hands. The patient was unable to hop or to walk on his heels. Some atrophy of the muscles which showed weakness was noted. There was definite tenderness of the calves and thighs. The pupillary responses were normal. The fundus was anemic but otherwise negative. The value for total protein in the spinal fluid was 160 mg per 100 c.c. with 2 lymphocytes per cubic millimeter.

The patient was one on whom Dr. Roth made skin temperature studies. The skin temperature of his toes was found to be higher than that of the fingers, at room temperature, in the cold room and in the warm room. Normal sweating of the feet did not occur. Normally the skin temperature is warmer in the fingers than in the toes. However, following lumbar sympathectomy, skin temperature is found to be higher in the toes than in the fingers and no sweating occurs. This would indicate that along with the picture of diabetic polyneuritis in this case there was also interruption of the function of the sympathetic nerves, probably due to an involvement of the autonomic fibres—a peripheral visceral neuritis.

The confused subjects of etiology and specific treatment in group 3, diabetic polyneuritis, have been purposely avoided. The usual factors mentioned are arteriosclerosis, repeated periods of poor diabetic control, infection, vitamin B or other dietary deficiency, institution of insulin therapy and associated orthopedic and mechanical causes. In general, the situation may probably be summed up in one of two ways: either diabetes somehow renders the nervous system abnormally susceptible to injury by the same etiologic factor, such as vitamin deficiency, infection, alcohol or pressure, which causes neuritis in nondiabetic persons or nondiabetic factors just mentioned injure the nerves and make them more susceptible to some as yet unexplained "diabetic" factor. In either case, the type and severity of the neuritic process seem somehow to be influenced by the diabetes.

I should like to emphasize again that the division of diabetic neuritis into the four groups of group 1, diabetes with pain, group 2, ischemic neuropathy, group 3, diabetic polyneuritis and group 4, diabetic visceral neuritis is presented as a working hypothesis only and not as a rigid or final classification. It is realized that the classification is probably over definite, that it necessarily has limitations and overlappings but it is hoped that the future studies of diabetic neuritis may be more valuable if cases of diabetic neuritis are thought of and grouped in some such manner as I have outlined.

DIABETIC NEUROPATHY Rudy, A. and Epstein, S.H. *Journal of Clinical Endocrinology* 5:92, February, 1945)

The authors present a review of 100 cases of diabetic neuropathy. The purpose of the study was to show that so-called diabetic neuritis or neuropathy is not, as is generally believed, exclusively a peripheral neuritis, but is also a generalized neurologic disturbance involving the entire nervous system. There is strong evidence to suggest that neuropathy is only one manifestation of vitamin B deficiency in diabetic patients and that the deficiency in most cases is secondary to metabolic disturbances in diabetes. The cases included in this study were followed for periods from one to ten years. Thirty-one cases had a peripheral neuritis, 26 patients had a myelopathy, 9 had signs of encephalopathy alone or combined with a myelopathy and 11 had a neurogenic bladder. Pain and sensory disorders were the most common symptoms and signs. Tendon reflex changes were found in 66 cases. Hyperreflexia was seen in 5. Sphincter disorders, especially of the urinary bladder, were present in 25 cases and 17 had some disorder of gait.

The role of diabetes in the development of the neuropathy is still obscure. The authors conclude, however, that diabetic neuropathy is a generalized neurologic disturbance. It is observed not only in the acute stage of diabetes but also soon after the control of the glycosuria and hyperglycemia, and in the chronic and even mild cases of diabetes. This neuropathy develops most frequently in patients over 50 years of age and is preceded or accompanied by marked loss of weight. Symptoms and signs of a vitamin B-complex deficiency are frequently associated with it. The vitamin deficiency is secondary or "conditioned," and it appears to be caused by the disturbed metabolism and at times by an associated chronic infection or other complication. A demonstrable dietary insufficiency is a factor in only certain cases. Complete recovery from the neuropathy is uncertain and slow but it occurs following prolonged therapy with vitamin B and control of the glycosuria and hyperglycemia.

MARIHUANA, BHANG OR GANJA, AN INTOXICANT

HERBERT S GASKILL, (*The Am Journ of Psychiatry* Vol 102, No 2 Sept 1945, p 202)

Marihuana or hashish (*Cannabis indica*) is an intoxicant which is derived from the hemp plant. It grows profusely in various parts of the world and is extremely common in India where it can be found growing wild in any field. Indians, particularly the coolie class, smoke it under the names of ganja and bhang. The dried leaves can be bought in any bazaar or from many peddlers, as well as gathered with almost no effort in the fields. The drug may be taken orally or smoked. The concentration of the crude resins in the oral forms is much greater and the effect is said to be more marked if the drug is taken in this manner than if the dried leaf is smoked. The experience here reported has been limited to those smoking the plant.

Large numbers of American soldiers stationed in India and Burma have had an opportunity to obtain marihuana since it is impossible to control its source. More than 150 patients have been seen in this hospital or in the out-patient clinic who have used the drug. The ratio of white to coloured is 1 to 20. Some of these individuals have been smoking marihuana for many years, but the largest group began after coming to this theatre. Nearly all who smoked "reefers" in the states report that the marihuana obtained here is much stronger and much more effective. Thus an opportunity has been afforded to study the effects which this intoxicant produces both on the novice and on habitual user. Diametrically opposed opinions have often been expressed concerning the harmful effects of this drug and its ability to produce addiction.

A statistical study has not been made but general conclusions based on the observation of these patients are presented.

The patients studied in this hospital who are known to smoke marihuana fall into two categories. The first are the occasional users who try it in an effort to relieve the boredom of their exist-

ence, particularly if stationed in one of the isolated jungle outposts, or who use it in an effort to reduce the tension and other neurotic complaints which have developed, or have become intensified, as a result of overseas duty. The second are the habitual users, those who have major personality defects, the immature, emotionally unstable individuals who have never found satisfactory expression for their instinctual life. A wide variety of personality defects, the melancholic, the mentally deficient, the early schizophrenic, the psychopath, may all find release in this drug, but the psychopaths form the great bulk of its users. Under this latter heading are included the aggressive, the paranoid, the schizoid, the emotionally unstable, the sexual pervert and the inadequate individuals who find the demands of reality beyond their capacity.

The first group is relatively unimportant. These soldiers indulge their taste only sporadically and rarely does it result in any anti-social behaviour which would endanger themselves or others. They merely take it for the temporary euphoria and amnesia which it produces. The other group is of greater importance. The criminal fringe of society is largely constituted from this type of individual who may become dangerous when marihuana has impaired his moral and intellectual judgment.

The effects of Marihuana smoking fall under two headings, the physiologic and psychologic. The physiologic symptoms are palpitation, nausea and vomiting, vertigo with ataxia, headache and tremor. In a few cases an intense and irresistible desire to sleep accompanies its use, the individual has to sleep until the effects of the drug wear off. In an occasional case a state approaching vaso-vagal syncope develops. The individual becomes light headed, loses consciousness and if examined at this time his pulse will be slow and at times irregular, the blood pressure falls and the extremities are cold and clammy. The pupils are variable, the deep reflexes vary from physiologic to hyperactive with clonus. Consciousness is regained gradually over a period of 10-15 minutes. The patient is unusually weak and complains of intense headache. The palpitation in some cases produces intense anxiety together with fear of dying which is sufficient to prevent their further use of the drug. The other unpleasant symptoms—headache, nausea and vomiting—likewise often act as a deterrent. These disagreeable somatic symptoms are either absent or so outweighed by the pleasant psychic effects in other individuals that they continue to use the drug.

The psychic effects are quite varied and, at least in part, depend on the type of the personality of the individual who uses the drug. The principal psychologic effects are the euphoria, the sense of well-being and the distortion of time perception. There is impairment of judgment both intellectual and moral. Boisterousness and impulsive behaviour are common. The tension under which the individual has been laboring is reduced since the demands of reality are diminished. The schizoid individual who constantly feels shy

and inferior either becomes less aware of his inadequacy, and thereby feels more capable of meeting the demands made upon him, or withdraws more into his world of fantasy. The former effect gives him a false sense of well-being, he feels more ambitious and more successful. He therefore has a distorted view of his ability and performance, which when checked objectively is found to be far from satisfactory. This tendency of the drug to allow fantasy free play and to remove normal inhibitions may have serious results in the paranoid and aggressive types. Often because of their defective judgment such individuals will commit criminal acts, which under ordinary circumstances they would be less likely to do. A great many stockade prisoners who have been examined to determine their sanity are habitual users of marihuana. When questioned about a criminal act they report that just prior to the incident they were smoking marihuana, their thinking then became blurred and they acted without full knowledge of what they did. Even under narco-analysis with sodium pentothal these amnesic periods cannot be recovered. In the Orient this tendency of the drug to result in criminal activities is well recognized. In the Malayan language, the term "run amuck" signifies this type of behaviour in a user of the drug. While there is no comparable term in Urdu, it is well recognized that the coolies, who for the most part are the chief users of marihuana in India, often become violent and aggressive under its influence.

In addition to the major criminal acts which occur as a result of marihuana intoxication there are many misdemeanors which follow its use. Thus the emotionally unstable individual becomes more impulsive and irritable. Despite his superficial bolsterousness and apparent good humor, he may become a bully and frequently gets into a fight with his associates. When he is at work his skill and judgment often are impaired by this intoxicant to the point where he damages equipment and endangers his own life and the lives of others. The sexual pervert who ordinarily cannot muster up enough courage to commit his act may do so under the influence of the drug. In addition there are the episodes of "running amuck" which occasionally occur. A typical example a negro soldier had been smoking marihuana in his bash. He suddenly got up from his bed where he had been day dreaming, seized his rifle and began firing it through the roof and the walls of the basha with total disregard for the safety of others. His associates quickly disarmed him. When seen by his medical officer a few minutes later he was dazed and confused, he appeared to be totally unaware of his surroundings and could give no account of this recent behaviour. He was given a sedative. When he awoke a few hours later he complained of severe headache, had no memory of the recent episode but was quite disturbed because he recognized the seriousness of his act.

While it is true that those psychopathic individuals who commonly smoke marihuana often exhibit abnormal behaviour without it, the tendency for a social or psychotic behaviour is greatly in-

tensified by its use. The relatively weak imperative to conform to reality is lessened by this drug and the inhibitions which ordinarily hold these persons in check, although imperfectly, are discarded. Marihuana like alcohol does not necessarily produce abnormal behaviour. The danger lies in the fact that immature and psychopathic persons use it to deaden their perception of reality and when under its effect their inhibitions and judgment are impaired with consequent increase in abnormal behaviour.

There has been considerable controversy as to whether the drug produces addiction. It certainly does not do so in the same sense that opium does because habitual users do not develop tolerance to the drug, nor do they have withdrawal symptoms when it is discontinued. Many of the patients seen here have used marihuana steadily over periods as long as 10 years, and yet rarely will they smoke it more than three to six times a day. Moreover when they are placed in a closed ward where all access to the drug is denied, they show no withdrawal symptoms. They resent being deprived of the drug and if they are at all honest, do not deny that they are going to use it again as soon as the opportunity presents itself. It is interesting to note that most of these individuals when they know they are coming overseas try to get a sufficient supply of "reefers" to last them during their entire voyage. In most instances they have underestimated the length of the trip and the supply runs out during the latter part of the voyage. However, they generally suffer no unusual symptoms as a result of this.

It has been said that individuals who use *Cannabis indica* in larger doses over long periods of time develop a typical psychotic reaction, which is accompanied by complete intellectual and physical deterioration*. Only one case has been seen here which approached this condition. This individual was a negro soldier who was brought to the hospital from the stockade where he had been taken shortly after his troop train arrived in this area. He came over as a casual replacement so that little was known about his past history. He had been a constant problem en route, completely undisciplined and subject to violent fits of anger. While in this hospital the patient was violent and aggressive, there appeared to be almost complete intellectual, moral and emotional deterioration. His behaviour varied from periods of apathy and indifference during which he was accessible but appeared to be capable of only the most elementary mental processes, to periods of acute delirium when he would attempt to injure himself and others. He said that he had been smoking "reefers" since he was a child. Whether this represented the end stage of prolonged use of the drug or not cannot be definitely stated without a complete history.

Since there are no withdrawal symptoms, management of these patients is quite different from that of narcotic addicts. The main problem has to do with the underlying psychopathology. In the case of the neurotic, superficial psychotherapy which attempts at

* Bouquet J. Marihuana intoxication. J.A.M.A. 124: 1010 (April 1, 1944).

developing insight into the causes of his tension and anxiety, is frequently of considerable help. However, in the case of deep seated personality maladjustments, cure is uncertain. Any improvement which might be hoped for would only occur after prolonged periods of retraining which are beyond the scope of an overseas hospital. In view of the generally poor prognosis as far as such patients are concerned even under opium treatment and environmental conditions, it is open to serious question whether such problems should be handled by the army psychiatrists who have so many acute problems which are the direct results of the stresses of the service.

SUMMARY

1 Marihuana does not produce addiction in the sense that opium and its derivatives do. Tolerance is not established and withdrawal symptoms do not occur. It is an intoxicant which temporarily produces euphoria, distortion of time perception and impairment of intellectual and moral judgment.

2 Its habitual users are largely emotionally immature individuals who are constantly frustrated in their attempts to find adequate instinctual expression. The fundamental problem is the abnormal personality.

3 Marihuana smoking creates an important problem since it often acts as the determining factor, turning the balance in the direction of a social behaviour rather than permitting the poorly integrated social conscience of such an individual to remain in control.

Book Reviews & Notices

THE 1945 YEAR BOOK OF GENERAL MEDICINE edited by C. F. Dick (Infectious Diseases), J. B. Amberson (Chest except Heart), G. R. Minot and W. B. Castle (Blood and Kidney), W. D. Stroud (Heart and Blood Vessels), G. B. Easterman (Digestive System and Metabolism). Chicago: The Year Book Publishers, Inc. pp. 708. price 3 U.S. dollars.

The 1945 Year Book of Medicine maintains the high standard established by the editors in the past. Every article bears the mark of careful editing and many articles are enlivened by editorial comments, some laudatory, some caustic. The abstracts are taken from journals all over the world and the year book may be taken as an index of the international medical work during the year, likely to be of practical use to the general practitioner. The illustrations, charts, indexing and printing all show the amount of care bestowed on the book production by the publishers.

The articles on Filariasis, Visceral Leishmaniasis, Kala-azar stimulating splenic anaemia, Newer aspects of Malaria, Diagnosis of Malaria will be of special interest to our readers.

Thatcher's experiments indicate a promising therapeutic value for the combination of sulfathiazole and methylene blue in the treatment of chronic genito-urinary infections caused by gram-negative bacteria. Very large doses of salicylates are likely to produce capillary damage and hypoprothrombinemia and fatal haemorrhages. The value of penicillin in the prevention and treatment of empyema appears

to be now established. The importance of infective hepatitis is stressed by a number of articles. The part played by flies in the spread of poliomyelitis is well borne out by the work of Ward, Melnick and Horstmann. The value of prostigmine in the treatment of poliomyelitis is shown in several articles. Penicillin is used in the treatment of intractable bronchial asthma where infection seemed to be an important etiologic factor. Penicillin has been successfully used in several cases of agranulocytosis as also pyridoxin (vit. B₆) intravenously, 100-200 mgm per day for 48 hours. The superiority of blood creatinine over urea nitrogen determinations as a prognostic sign in patients with severely impaired renal function is stressed by Myers. Gilbert confirms the value of subcutaneous administration of atropine immediately after coronary occlusion in reducing the mortality, which can be further reduced by using aminophyllin or papaverine with atropine. Distention of an animal's stomach with a balloon causes a decrease in coronary flow, which does not follow when the vagi are cut or atropine is administered, thus proving that the decreased flow is due to a reflex vaso-constriction. This will explain why many cases of coronary occlusion occur after a heavy meal and why anginal pain is brought on when abdomen is distended with gas and there is relief by expulsion of flatus. The discussion on the use of digitalis in myocardial infarction is timely and helpful. Levine's article on Rest, Bed Rest and Heart Disease in a sound exposition of mechanisms of circulation and hazards of prolonged bed-rest.

Reflections and Aphorisms

PHILOSOPHIA MEDICI

We, physicians, ought to pause every now and then to consider our functions and our duties and our methods, each in turn, for only by so doing shall we keep our house in order and set a check to precipitate building or careless refurbishing.

The first function of the doctor is to become a good student of nature, and particularly of human nature, for whatever the character of his training, his life as a practicing physician, surgeon or specialist will be devoted to the study of a very complex animal in a great variety of environments. The whole biology of man in health and disease is his subject in whatever directions he may later elect to limit it. To this study anatomy, physiology and pathology and many other sciences make their important contributions, but without the field—study of living man in all his variations of age, sex, race, physique and temperament, and without a close attention to his environment, the primary sciences would be of little help to the doctor or his patients. Observation, sympathy and the ability to make close contacts without inspiring fear or suspicion are as necessary for the man-watcher as for the bird-watcher.

A second function of the doctor is to invoke all appropriate forms of scientific knowledge to assist his field studies, while he also learns the limits of their applicability, when and where to employ them and when to dispense with them.



A third function, on the basis of diagnosis or "through knowledge" and of prognosis or "foreknowledge," is to develop a rational plan of healing which must take into proper account the needs of body and mind, of whole and part

We doctors have duties to the patient, to the relative and to the community, whose servants we are and whose teachers we must much more consciously become. Like the scientists we have not yet appreciated fully our obligations to individual man and to the State. To both we could give more guidance and increasing help as science improves our powers. The preventive field could be fruitfully explored in many new directions. Instruction in the art of living healthily must become a more important concern than that of discovering new treatments for preventable diseases. To give the greatest help the profession must more generally deserve the trust and confidence which individuals and communities have felt for the best type of doctor in all ages. There has been an appreciable loss of public trust in recent years, and this can be traced in part to the growth of certain materialism, and in part to a waning of intimate human sympathies and to a failure to replace old professional faith by a new faith founded on an integration of the old and the new knowledge.

—JOHN A RYLE, MD

Medical News & Notes

ISOLATION OF MYCOBACTERIUM LEPRAE by R. Row. In continuation of the announcement in the January number of the *Indian Physician* (p. 26) we are in a position to inform our readers that Dr. R. Row has now confirmed his previous findings by pursuing the investigation further, he has been also able to isolate *Mycobact. Leprae* in four more cases, in succession, of leprosy (including one of tuberculoid type) and that he has in addition succeeded in isolating in culture and subculture, the *mycobacterium Stefanski* of "Rat Leprosy" by employing the same technique of symbiosis in culture. We feel indebted to this worker for introducing altogether a new conception of utilising a natural biological phenomenon, in bacteriological technique concerned with the isolation in culture of a micro-organism considered unculturable, by symbiosing it with another parasite known to be culturable. His experiments demonstrate that in symbiosis one growing micro-organism can not only set another starving microbe on its feet by sharing with its helpless companion its own food from the nutrient material but can even make it thereby stand firmly on its legs and grow on its own, independent of further support.

WANDER JUBILLEE VADEMECUM—Dr. A. Wander (India) Ltd., as sole representatives for Dr. A. Wander S.A. Berne (Switzerland), have sent us a copy of the *Wander Vademecum*, containing information on all Wander specialities already marketed or just being introduced in India. The *Vademecum* presents, in a concise form, all that the practitioner should usefully know about the composition, indications and dosage of Wander medicaments. Physicians who have not received their copy can obtain it on application to Dr. A. Wander (India) Ltd., Post Box 1125, Bombay—1.

Original Contributions

ISOLATION OF MYCOBACTERIUM LEPRAE IN CULTURE

R ROW, D.Sc., M.D. (Lond)

Before proceeding with the lecture, I crave your indulgence for a few moments for one or two personal references

I am grateful to Col Jelal Shah for the unique opportunity he has given me to come to my dear old Alma Mater just on the morrow of her centenary which we have been celebrating, and place before her, my latest contribution to science, however insignificant, for her acceptance as a small token of my deep homage to her for all the innumerable benefits, I have been fortunate to receive at her hands ever since I entered her portals in 1888

Now to come to the subject before us, recently a large body of investigators have engrossed themselves with a natural biological phenomenon "Antibiosis" which implies the inhibition or destruction of some of the living-micro-organisms found in association together in a common environment, e.g., a nutrient culture medium This has been so, since the brilliant discovery of Penicillin by Flemming, but particularly after Flory and Chain and others in Oxford made it possible for practical application in therapy Be it noted that Flemming himself applied Penicillin to eliminate some Gram-positive micrococci, e.g., Staphylo, Strepto, Pneumococci which he found as constant contaminants in his attempts at isolating the Influenza bacillus making use of the strong antibiotic quality of this substance, for some time before the period referred to This enthusiasm was not confined to England and America only, it spread to Bombay and even to my own little Laboratory where some of my assistants were attracted even at the sacrifice of their legitimate duties to the Singhanee Hospital to work in search of the philosopher's stone out of a large number of moulds

But fortunately I had no attraction for a phenomenon aiming mainly at destruction of living germs On the contrary in my search for a suitable nutrient for Mycobacterium leprae after failure after failure for the last 35 years, it induced me to be on the look out for altogether another biological phenomenon concerned in preservation

A lecture delivered at the Grant Medical College, Bombay, on 20th March 1946, with Sir S S Sokhey in the chair

When examined a week later, in a fresh drop, it showed a large number of active flagellates and many rosettes of these, of different sizes, the drop after drying and staining in Zeihl-Neelson presented a most surprising spectacle in as much as it showed a marked proliferation of the acid-fast bacilli in close contact and inside the Leishmanial rosettes, and individually the bacilli were fatter and longer than those seen in the smears of the original lesions vide Figs 1 and 3

A week later, all these characters were well maintained with increased proliferation in the denser masses of rosettes now overcrowded by the Myco leprae, their own morphology being obscured by the bacterial overgrowth vide Fig 4 It was now felt that an attempt might be made to transplant the growth in the fluid medium, on the surface of solid media, viz

(1) On the surface of the solidified Haemoglobinised saline agar described by me⁷ in 1930, with a view to obtain a symbiotic culture on a solid surface at 20° C

(2) On the surface of a glycerinated potato, with the hope of isolating the acid-fast bacilli at 37° C and free from Leishmania which cannot grow on this medium and at this temperature

The gross and microscopic characters of the above made cultures on solid media.—

(1) After 10 to 15 days incubation at 20° C, the symbiotic culture on the solid haemoglobinised saline agar presented a translucent film on the surface consisting mainly of Leishmania but the film was interspersed with a good many fine yellow colonies which when examined microscopically after staining with Zeihl-Neelson, were mainly made up of acid-fast bacilli which had distinctly altered in size, in the individuals being shorter than those found in the parent symbiotic fluid culture two weeks previously These colonies were planted on solid glycerinated agar and on glycerinated potato and in two weeks time yielded pure culture at 37° C on the surface having a faint yellow growth, now made up of coccal forms and some coccobacillary intermediaries, but all acid-fast

2) The potato culture at 37° C also presented a distinct yellow film by two weeks, this film grew thicker and at the end of four weeks presented distinct tubercle like masses heaped up on the surface, the whole being by now distinctly canary yellow The thick and abundant growth was moist but not glistening, and dull but not as dry as a tubercle bacillary culture It is easily and wholly dislodged from the potato surface with a glass loop, and easily gathered as such or for saline suspensions Microscopically the culture is made up of fine uniform cocci like staphyloes or streptococci, but all acid-fast They yield subculture on solid glycerine potato resembling the parent in every respect They are also culturable in a synthetic glycerinated saline fluid with some amino-acids as its nitrogenous constituent and the cultures appear as uniform turbidity in less than a week without any scum or deposit Mi-

ROW—ISOLATION OF MYCO LEPRAE

PLATE I

THE INDIAN PHYSICIAN—APRIL, 1940

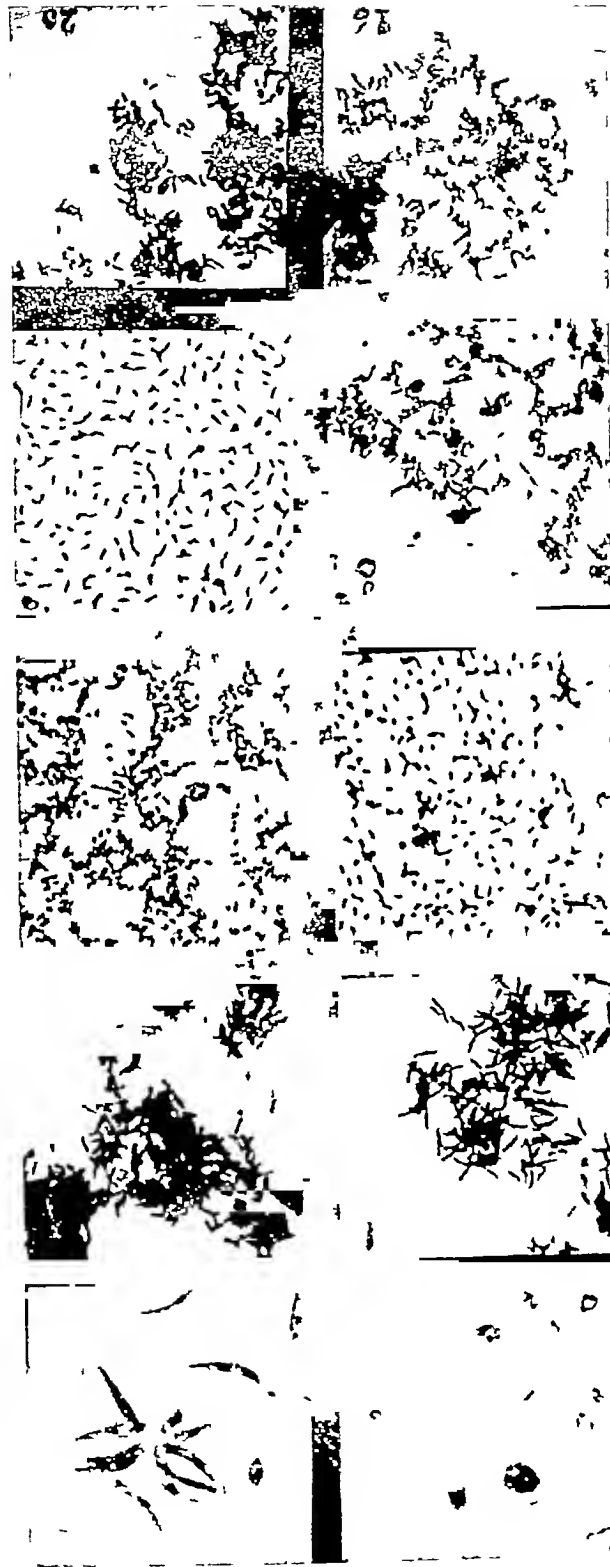
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Human Myco leprae (case I 1) slides showing—

Fig 1 Smear from Lepromin (L.I.)

2 Felsmanin in rosette

3 One week symbiosis in Fluid Haemoglobin at 20 C

4 Two weeks symbiosis in Fluid Haemoglobin at 20 C

5 Pure isolated bacillary culture on Glycerinated agar at 37 C.

6 Pure isolated bacillary culture on Glycerinated potato

7 Pure subculture from above in synthetic glycerinated broth

8 Symbiotic culture on solidified Haemoglobin Saline agar at 20 C.

9 Pure isolated Myco leprae on agar at 37 C. (canary yellow)

10 The same as 9 but in symbiosis in Fluid Haemoglobin at 20 C.

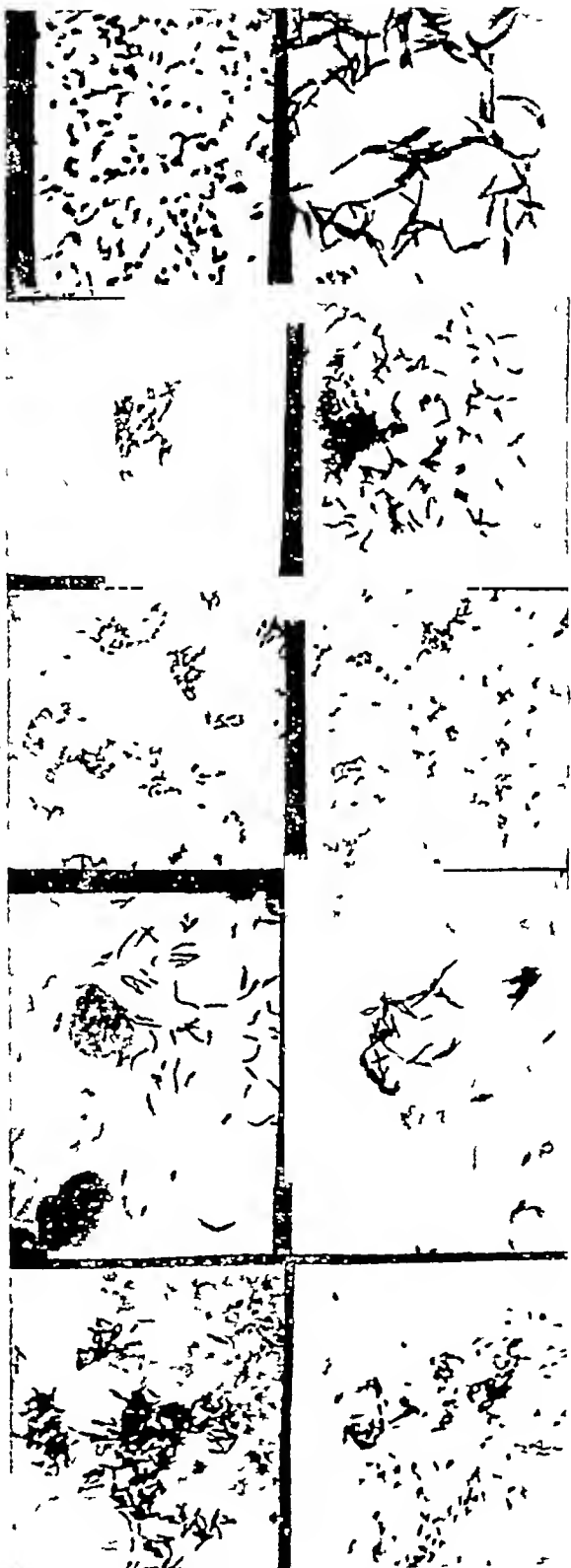
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Fig 11 Symbiotic culture in
Fl Hb at 20°C (5 weeks)
12 Same as (11) but re-
peatedly symbiosed at 20°C
to show the nutritonal value
of symbiosis

Case Z
13 Smear from Leproma
14 One week symbiosis in
Fl Hb at 20°C

15 Pure isolated Myco
leprae on Glycerinated po-
tato
16 Symbiotic culture on
Solid Haemoglobin Saline
agar at 20°C.

Myco stefanski Rat (prosy)
17 Smear from Splen of
mouse showing Myco
stefanski
18 One week symbiosis in
Fl Hb at 20°C

19 Two weeks symbiosis
in Haemoglobin saline at
20°C.
20 Pure isolated Myco
stefanski on Glycerinated
potato at 37°C.

microscopically they are like streptococcal and staphylococcal in appearance but always acid-fast, and subculturable on all solid and fluid media employed, vide, Fig 7 In short the pure culture at 37° C on solidified surface as also in glycerine broth are made up of coccal acid-fast micro-organisms and thus bring out the pleomorphic characters of the parasite In culture, these coccal forms are, however, reconverted into bacillary forms by symbolising them at 20° C, repeatedly vide Figs 9 and 10

Before leaving the subject of the culture in fluids during symbiosis at 20° C It may be pointed out that as the culture ages, the long bacillary forms shorten week after week, after the third week, until they become coccobacillary, these coccobacillary forms are also reconvertible into longer bacillary forms by repeated symbiosis at 20° C in fluid media, vide Figs 9, 10 and 11, 12

To sum up—pure cultures are obtained of *Myco leprae* by preliminary symbiosis at 20° C with *Leishmania* in culture when the bacilli grow fatter and longer The pure cultures are pleomorphic and ultimately settle down into fine coccal forms, with coccobacillary intermediate stages They are always acid-fast Sub-cultures are easily made from the parent cultures

The observations above recorded indicate that in symbiosis the *Leishmania* not only sets a helpless parasite on its feet by its sharing the split products of the nutrient material but by symbiosis it is capable of enabling its weaker companion to stand firmly on its legs and grow on its own, independent of further support

By employing the same symbiotic technique 4 more *Myco leprae* have been isolated from four cases in succession in culture on Gly Potato, etc They are practically of the same character as the first turning ultimately canary yellow when about one month old The pleomorphism seen is exactly the same in all, the bacilli growing in fat and long forms in the first two weeks of symbiosis at 20°C and then into coccobacillary forms later, and ultimately settling down into coccal forms both in older symbiotic cultures as well as in the pure cultures isolated on Gly Potato, Gly Agar, and broth at 37° C Vide Figs 13, 14, 15 and 16

Myco stefanski in culture—Rat leprosy is a natural infection found occasionally in rats, and is caused by *Myco stefanski*—very like the *Myco leprae* and equally unculturable in the ordinary way The disease is transmissible from rat to rat or rat to mouse by subcutaneous or intraperitoneal inoculation, the animals taking the infection in 4 to 6 months or longer, by which time almost all the internal solid organs and the lymphoid tissue become involved with definite and massive lesions The animal from which the culture was attempted by me was inoculated on 27-10-45 and was killed on 11-2-46 P.M the liver and the spleen were studded with small translucent boiled sago-grain like tubercles and from one of these a weak suspension was made for symbiosis with *Leishmania*, and the Cultures, and Subcultures were carried out by the same technique employed for the isolation of *Myco leprae* and the results were practically identical with them The

final isolated culture on Gly Potato becomes also pale yellow—it is perhaps a little slower in growth than *Myco leprae* but finally it settles down like it into coccal acid-fast forms in pure culture (Vide Figs 17, 18, 19 and 20)

REMARKS BY SIR S S SORHEY

Opening remarks—Dr R Row needs no introduction at any hands. He is the doyen of medical research in India and has inspired most of us by his selfless devotion to research. He was not only as illustrious scholar of this medical school where we were meeting today, but occupied the chair of Pathology for a number of years with great distinction. The subject on which he is going to speak today is of the greatest importance to the world of science. Advance in the control and treatment of leprosy has been held up by our inability to propagate the organism of leprosy in the laboratory and our inability to infect laboratory animals. A number of workers have claimed, from time to time, to have grown the organism in the laboratory, but their methods of cultivating the organism have not proved successful for any sustained growth of the organism. Dr Row, who has worked for many years on the subject, will describe to you today a new method of cultivating the organism in the laboratory which breaks entirely new ground. I call upon Dr Row to tell you of his work himself and not anticipate him.

Closing remarks—It has been one of the most exciting and lucid discourses I have had the privilege of being present at. Although Dr Row had done me the honour of telling me of this work from time to time, I am glad to be present at this masterly presentation which has so clearly brought out the implication of his new approach to the problems of cultivating the leprosy organism. The several cultures and serial subcultures which Dr R. Row has been able to make so far and in five cases in succession, put the symbiosis of *Leishmania tropica* (or *donovani*) and *Mycobacterium leprae* on a fairly firm basis. His work is, of course, continuing. What is equally interesting is that he has been able to propagate the organism of rat leprosy. This will enable him to infect rats and thus satisfy the 3rd and 4th of Koch's postulates. It is further to be hoped that now that Dr Row can cultivate *Mycobacterium leprae* in fairly large amounts, it may be possible for him to infect mice or rats, with massive infective doses, and thus put his discovery on a still firmer basis and open out a very wide field for further research.

I know he intends doing all this, and we are grateful to him to have taken us into the secret at this stage. The only way we can honour him is to take up this work and repeat it and make the fullest possible use of it to take the studies of leprosy further afield.

I congratulate Dr Row on your and my behalf for this great piece of research, which I trust, will become an important milestone in man's conquest of leprosy. I also thank him for giving us this discourse and in his usual selfless way taking us into the secret. You will all join me in wishing him success in carrying his experiments further.

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THE AURICULAR WAVE

AN EXHAUSTIVE INQUIRY INTO THE PHYSIOLOGICAL AND PATHOLOGICAL VARIATIONS OF THE P WAVE (OR AURICULAR WAVE) OF THE ELECTROCARDIOGRAM

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and
E P BHARUCHA, M D (Bom)

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(Continued from p 48)

STATISTICAL DISTRIBUTION OF P WAVE ABNORMALITIES:

The majority of Electrocardiograms taken at the K.E.M. Hospital from 1937-1944 (both years inclusive) were studied with reference to the incidence of different forms of P Wave abnormalities

Out of a total number of 631 cases studied, 190 cases showed abnormally large P Waves* giving an incidence of 30.2 per cent. The distribution of these is shown in Table VII

TABLE VII

	Total No of cases	No of abnormally high P Waves.	% Incidence
Mitral Stenosis	47	28	59
Mitral Regurgitation	43	19	44
Aortic Regurgitation	61	21	34
Hypertension	20	10	50
Coronary Sclerosis & Angina	54	15	30
Coronary Occlusion	72	15	21
Cardiac Failure	123	38	31
Congenital Heart Disease	20	5	25
Neuro Circulatory Asthenia	30	11	22
Extrasystoles	21	5	24
Bradycardia	22	5	22
Infections (Pneumonia Typh Diph. Acute Rheum, etc.)	58	15	30
Thyrotoxicosis	12	2	16
Beriberi	18	1	7
Anaemia†	20	1	5
	631	190	

Abnormally low P Waves (viz according to Pardee less than 1 mm in all the three leads), were found in 79 out of a total of 631 cases studied. The distribution of these small P Waves is shown in Table VIII

TABLE VIII

	Total No of cases.	No of abnormally small P Waves	% Incidence
Mitral Stenosis	47	4	8
Mitral Regurgitation	43	2	4
Aortic Regurgitation	61	5	8
Hypertension	20	2	10
Coronary Sclerosis & Angina	54	5	10
Coronary Occlusion	72	4	5
Cardiac Failure	123	12	9
Congenital Heart Disease	20	8	10
Neuro Circulatory Asthenia	30	5	10
Extrasystoles	21	4	20
Bradycardia	22	5	23
Infections (Pneumonia, Typhoid Diphtheria, acute Rheumatic fever)	53	9	21
Thyrotoxicosis	12	3	25
Beriberi	18	5	61
Anaemia†	20	9	45
	631	70	

* According to Pardee's criteria, viz, P Waves larger than 1 mm in Lead I and over 2 mm. in Lead II

† The high incidence of abnormally low P Waves in Anaemias is rather striking

THE P WAVE IN VALVULAR DISEASES OF THE HEARTS

1 The P Wave in Mitral Stenosis

(a) *Amplitude* In the present series of 47 cases of Mitral Stenosis with normal rhythm, 28 cases had abnormally large amplitudes of P Waves in one or more leads according to Pardee's Criteria (viz figures of over 1 mm in lead I or over 2 mm in lead 2 were considered abnormal) This incidence works out at 59.1 per cent which is much smaller than that given by White & Burwell (viz 77 per cent of abnormally large P Waves in 57 cases of Mitral Stenosis) and by Alexander et al (84 per cent in a series of 58 cases) In seven of our cases of Mitral Stenosis the P Waves were unduly large in leads one and two (giving an incidence rate of 15 per cent) In 18 cases, the P Wave was unduly large in lead I only and in three cases in lead II alone

The maximum amplitude of P for Lead I in our series was 2.25 mm in case No 47 and for Lead II was 4 mm in case No 39 The amplitude of P Waves in Lead II was found to be 3 mm or over in 6 out of our series of 47 cases (giving an incidence rate of 12.8 per cent) This small incidence of "very high" P Wave in Lead II offers quite a contrast to the high incidence rate of 68 per cent given by Alexander et als for their Mitral series

Comparison with normal (Table IX) The Mitral values for amplitude have been compared with normal figures worked out for Indian Subjects in 1940-41 by one of us (R J V) The average value for P was found to be 0.24 mm more in Mitral Stenosis than in normal cases in Lead I, 0.36 mm greater in Lead II, whereas in Lead III the average value was actually found higher in normal cases by 0.65 mm

TABLE IX. Comparison of P Wave amplitudes in Mitral Stenosis with normal figures

	NORMAL			MITRAL STENOSIS		
	I	II	III	I	II	III
	mm	mm	mm	mm	mm	mm
Average	0.89	1.35	0.755	1.13	1.71	0.69
Minimum	-0.3	-0.2	-2	-1.5	-0.75	-2.25
Maximum	2.3	3.1	3.2	2.25	4.0	2.00

(b) *Duration of P*—In our series of 50 cases of Mitral Stenosis with normal rhythm, 23 cases out of 50 had increased duration of P Wave in one or more of the 3 standard or limb leads (giving an incidence rate of 46 per cent) According to Pardee, an increased duration of P is found in 85 per cent of records of Mitral Stenosis This figure is much higher than that found in our series (viz 46 per cent)

In two cases, the duration of P Wave was excessive in Lead I alone (the maximum duration being 0.12 sec in case No 38), in 2

cases, in Lead II alone (Maximum duration being 0.12 sec in both cases), in 2 cases, in Lead III alone (Maximum duration being 0.12 sec in case No 2)

The P Wave duration was excessive in both Leads I and II in 10 cases (20 per cent of the series) in Leads I and III in 1 case only, in Leads II and III in 5 cases (10 per cent of the series) and in Leads I, II, III in only one case (case 29)

The highest value for P Wave duration was found to be 0.14 sec in Lead I, (cases 15, 20, & 29), 0.16 sec in Lead II (cases 27 and 29), 0.16 sec in Lead III (Case 7)

TABLE : A Comparison of P Wave Duration in Mitral Stenosis cases with Normal Values

	NORMAL			MITRAL STENOSIS		
	I	II	III	I	II	III
Average	mm 0.0705	mm 0.082	mm 0.077	mm 0.09	mm 0.1	mm 0.08
Minimum	0.04	0.03	0.03	0.04	0.06	0.04
Maximum	0.15	0.15	0.14	0.14	0.16	0.16

A comparison of P Wave duration values with normal figures for Indian Subjects reveals an average value of P Wave duration definitely larger in the Mitral group than in the normal group, in Lead I, the average duration being 0.0105 sec greater in the mitral group, in Lead II—0.008 sec greater and in Lead III, 0.003 sec greater in the mitral group

Relationship of P Wave duration to Amplitude discussed

Alexander et al could not find a single case of Mitral Stenosis with increased duration but normal amplitude of P Wave. In our series, however, there were 4 cases (cases 7, 32, 34, and 50) with normal P Wave amplitudes but prolongation of P Wave duration. In case 7, the P Wave duration was as high as 0.14 sec in Lead II and 0.16 sec in Lead III and yet the amplitude of P was within normal limits in all the three Leads. This serves to emphasize the importance of estimating the duration of P Wave in cases of Mitral Stenosis specially in cases where there is no increment in the amplitude of the wave, this may be the only electrocardiographic indication of Auricular hypertrophy in cases of this type. In our series of Mitral Stenosis cases, there were only 9 cases where the duration of P was found normal with increase in amplitude of that wave. In other words great majority of cases with high amplitude of P also reveal an increase in duration.

(c) *Notching of P*—This was present in 31 cases in one or more leads. As the total number of cases of Mitral Stenosis studied from the point of view of notching was 41, this gives an incidence rate of 75.6 per cent. This incidence is strikingly high when compared to the figure of 60 per cent given by Pardee for notching in Mitral Stenosis.

In 11 cases notching was present in one lead alone, 3 times in lead I, 4 times in Lead II, and 4 times in Lead III.

In 10 of our cases, notching was present in 2 Leads, twice in Lead I and II, 7 times in Leads II and III and in one case in Lead I and III. Notching was present in all three Leads in 10 cases of the present series (Incidence of 25 per cent)

II The P Wave in Mitral Regurgitation —

(a) *Amplitude*—43 cases of mitral regurgitation with normal rhythm were studied, and of these, 19 cases had an abnormal amplitude of P Waves (criteria given above). Of these 19 cases, 14 had abnormal values of P in Lead I (the maximum value of P in Lead I was 2.0 mm in cases No 2, 11, 12, 24 and 25,) in Lead II alone, an abnormally high P Wave was found in three cases, the maximum value being 4.0 mm in cases No 12 and 31. Leads I and II showed unduly large P Waves in 2 cases only.

Comparison of values with normal—In Table XI the figures for Mitral Regurgitation are compared with normal figures for Indian Subjects (worked out in 1940-41). The average value of P was found to be 0.11 mm more in Lead I, 0.17 mm more in Lead II, and 0.05 mm more in Lead III—in cases of Mitral Regurgitation than in normal subject.

TABLE XI Comparison of amplitude in Mitral Regurgitation with normal values

	NORMAL			MITRAL REGURGITATION		
	I	II	III	I	II	III
	mm	mm	mm	mm	mm	
Average	0.89	1.35	0.755	1.10	1.52	0.77
Minimum	-0.3	-0.2	-2.0	0.25	0.25	-0.25
Maximum	2.3	3.1	3.2	2.0	4.0	2.5

(b) *Duration of P in Mitral Regurgitation* Out of 43 cases of Mitral Regurgitations studied, only 13 cases had a prolonged duration i.e. (over 0.1 sec in any Lead) in one or more of the limb leads. This gives a percentage value of 30.2 per cent.

In 3 cases, the duration of P was prolonged in Lead I alone (the maximum duration being 0.2 sec in case No 7). In 4 cases, in Lead II alone (the maximum duration being 0.16 sec in case No 10), in two cases in Lead III alone (the maximum values being 0.12 sec in both cases).

The duration of P was prolonged in both Leads I & II in 2 cases (4.7 per cent) and in both Leads II & III in two cases (4.7 per cent) of the present series.

The highest values of P Wave duration was found to be 0.2 sec in Lead I (Case No 7) 0.16 sec in Lead II (Case No 10) and 0.13 sec in Lead III (Case No 28).

TABLE XII
Comparison of durational values of P Wave in Mitral Regurgitation with normal figures

	NORMAL			MITRAL REGURGITATION		
	I	II	III	I	II	III
Average	0.0795	0.092	0.077	0.078	0.113	0.070
Minimum	0.04	0.03	0.03	0.04	0.02	0.04
Maximum	0.15	0.15	0.14	0.20	0.16	0.13

Comparison with normal values A comparison of average P Wave durational values with normal figures shows no definite in-

crease in the Mitral Regurgitation group Only in Lead II is the duration longer in Mitral Regurgitation (by 0.11 sec) In the other Leads the values were normal or higher

Relationship of P Wave duration to amplitude In the present group of cases, 7 instances were found (7, 9, 10, 17, 20, 36 and 37) where the duration was prolonged with normal amplitude of P Waves This seems to bring out even more clearly than before mentioned, the value of estimation of the duration of the P Wave where the amplitude is normal In a case where the P Wave is suspected of being abnormal

The reverse of the above viz abnormal amplitude with a normal P Wave duration was found in 13 cases which is quite in contrast with the findings in Mitral Stenosis where the two factors had a direct relationship

(c) *Notching of the P Wave in Mitral Regurgitation*—Out of 35 cases of Mitral Regurgitation in our series, 21 cases showed notching in one or more of three standard Leads, viz, 60 per cent In 10 cases notching was present in one Lead alone, 3 times in Lead I, five times in Lead II and twice in Lead III Notching was present in two leads in 10 cases of this series, 6 times in Lead I and II, three times in Leads II & III, and once in Leads I & III Only one case showed notching in all three Leads

III The P Wave in Aortic Regurgitation —

In the Aortic Regurgitation series of 61 cases, there were 21 with abnormally large P Waves in one or more Leads (According to Pardee's Criteria) The incidence of large P Waves in the Aortic Regurgitation series works out as 34 per cent In 11 cases they were abnormally large in Lead I alone, in four in Lead II and in 6 cases in Leads I & II

The maximum amplitude of P for Lead I was +3.0 mm, the minimum—0.5, and the average for the series worked out at 0.95 mm For Lead II, the figures were as follows Maximum +5.5 mm, minimum —2.5 and average +1.34

Comparison with normal The values of P Wave amplitude in Aortic Regurgitation have been compared with normal figures and the following facts have emerged from this comparison The average value for P was found to be 0.06 mm more in Aortic Regurgitation cases than in normal in Lead I In Lead II the two figures were almost identical (0.01 mm more in the normal cases) In Lead III, 0.465 mm larger in Aortic Regurgitation than in normal cases (See Table XIII)

TABLE XIII
Comparison of P Wave amplitude in Aortic Regurgitation with normal figures

	NORMAL			AORTIC REGURGITATION		
	I	II	III	I	II	III
Average	mm 0.89	mm 1.35	mm 0.755	mm 0.95	mm 1.34	mm 1.02
Minimum	—0.3	—0.2	—0.2	—0.5	—2.5	—1.5
Maximum	2.3	3.1	3.2	3.0	5.5	3.6

IV The P Wave in Aortic Stenosis

As the present group of electrocardiograms included only five cases of Aortic Stenosis, no values could be taken for them

P WAVE IN THE CORONARY HYPERTENSIVE GROUP —

I The P Wave in Hypertension

Amplitude

In our series there were only 20 cases "labelled" as Hypertension. Of these 10 cases showed abnormally large P Waves (according to the above-mentioned criteria. This gives the surprisingly high incidence of 50 per cent. However, as the number of cases studied is a small one, too much emphasis should not be laid on this finding. Of these 10 cases of Hypertension with abnormally large P Waves, 8 were unduly large in Lead I, one in Lead II and one in Leads I and II.

The maximum amplitude of P for Lead I was 2.0 mm (In case No. 6) and 2.5 mm in Lead II (Case No. 5). This finding seems to point to the fact that though the number of cases of hypertension with large P Waves is quite high, the values of P are just outside the range of the maximum normal and do not compare with those of Mitral Stenosis.

Comparison with normal (Table XIV)

As in the other groups the amplitude values of the Aortic Regurgitation series are compared with normal figures. The average value of P was found to be 0.03 mm higher in Lead I than the corresponding average value for normal cases. In Lead II was 0.15 mm higher in Aortic Regurgitation whereas in the Lead III, the normal value was 0.065 mm in excess of the corresponding Aortic Regurgitation one.

TABLE XIV
Comparison of P Wave amplitude in Hypertension with normal figures

	NORMAL			HYPERTENSION		
	I	II	III	I	II	III
Average	mm 0.89	mm 1.35	mm 0.785	mm 0.92	mm 1.5	mm 0.68
Minimum	—0.3	—0.2	—2	+0.05	+0.5	—0.5
Maximum	2.3	3.1	3.2	2.0	2.5	2.0

II The P Wave in Coronary Sclerosis and Angina —

Amplitude

The present compilation included 54 cases under the heading of Coronary Sclerosis & Angina. Of these cases, 15 showed abnormally large P waves according to Pardee's criteria giving an incidence of 30 per cent. Of these cases, 13 showed the abnormality in Lead I and 2 cases in Lead II.

The maximum amplitude of P in Lead I was 2.25 mm and in Lead II —3.0 mm.

Comparison with normal (Table XV)

When compared with normal Indian figures, the average values of P in Lead I was 0.1 less, in Lead II —0.08 mm more and in Lead III —0.105 mm more in the Coronary Sclerotic group than in the normal group.

TABLE XV
Comparison of P Wave amplitude in Coronary Sclerosis and Angina Pectoris with normal figures

	NORMAL			CORONARY SCLEROSIS AND ANGINA		
	mm	mm	mm	mm	mm	mm
Average	0.89	1.35	0.755	0.70	1.44	0.86
Minimum	-0.3	-2.0	-2	+0.25	+0.25	-4.5
Maximum	2.8	3.1	3.2	2.25	3.00	2.00

III P Wave in Coronary Occlusion —

Amplitude —

Of the 72 cases of Coronary Occlusion studied, 15 cases had abnormally high P Waves giving an incidence of 21 per cent. Of these 11 cases showed abnormality in Lead I, two cases in Lead II and two cases in Leads I and II.

The maximum amplitude of P for Lead I was 2.00 mm, minimum - 0.25 mm and the average for the series worked out at 0.84 mm. For Lead II the figures were maximum 3.75 mm, minimum 0.5 mm, average 1.29 mm.

Comparison with normal —

TABLE XVI
Comparison of P Wave amplitude in Coronary Occlusion with normal figures

	NORMAL			CORONARY OCCLUSION		
	I	II	III	I	II	III
	mm	mm	mm	mm	mm	mm
Average	0.89	1.35	0.755	0.84	1.29	+0.00
Minimum	-0.3	-0.2	-2	-0.25	+0.5	-0.5
Maximum	2.8	3.1	3.2	2.00	3.75	2.00

When compared with normal Indian figures, the average value of P was 0.05 mm less in Lead I, 0.06 mm less in Lead II and 0.155 mm more in Lead III in the coronary Group than in the normal cases.

SUMMARY

(1) The above paper presents a detailed theoretical study of the auricular or P-wave of the Electrocardiogram under physiological and pathological conditions.

(2) An analysis is undertaken of a fairly large series of Electrocardiogram from the files of the K.E.M. Hospital, Bombay with a view to determine the various alterations of the P-wave in different pathological conditions affecting the cardio-vascular system.

(3) The following are a few of the conclusions arrived at from the above study: (a) That in cases of Mitral Stenosis, the P-wave duration may be the only electrocardiographic evidence of auricular hypertrophy, the classical sign of "large P-waves" being absent. (b) The high incidence of P-wave abnormalities (50 per cent) in cases of Hypertensive heart disease in our series of electrocardiograms deserves attention. (c) The low incidence in our series of P wave abnormalities in cases of Thyrotoxicoses (only 16 per cent) is not in conformity with the present day teaching and requires further investigation as the number of cases studied is small. (d) The high incidence of "low P-waves" (45 per cent) in our series of cases of anaemias is striking. However, the actual P-wave values in these cases have not been considerably below normal as for instance in cases of Beri-beri.

PROLAPSE OF THE RECTUM

G M PHADKE, FRCS (Eng)

My interest in this subject was created chiefly by the pathetic story of a middle-aged man, who had suffered from this disabling and annoying condition for a number of years. He was operated upon on two occasions previously by different methods and by two different Surgeons. The massive prolapse recurred four to six months after each operation. The repeated prolapse interfered very frequently with his work and being the only wage earning member of the family he had become despondent and consequently had gone down considerably in health.

Round about this time Graham's article on massive prolapse appeared in *Annals of Surgery* about the middle of 1942. The arguments given in that article appealed to us so much that it was decided to give that method a trial in preference to other methods of treatment for prolapse of the rectum. Seeing the satisfactory results in two of the early cases in my unit, the above mentioned man was operated upon by the same technique. This was 1 year and 10 months ago. So far the condition has not recurred. He is very happy about the end result and is at present working as a driver in the Bombay Fire Brigade.

The above subject cannot be discussed without considering the changes that time has wrought with three tail muscles to prepare the caudal end of the abdominal cavity to meet the extra demands of support in the upright position of man. In the words of Barrett the three muscles have exchanged length, grace and agility to make the whiplash of the tail, for breadth, compactness and stability that makes the abdominal floor a bulwark of strength and yet a facile passage for three important tracts which lead from the abdomen to the external world. These muscles have been modified and have become fused with the adjacent muscles and fascia to make a broad musculo-fascial plate which forms the lower wall of the abdomen, the pelvic-floor with tight clefts through which three important tracts pass. These latter are grasped with snugly fitting musculo-fascial structures which discussate with the structures of the tube in such a way as to allow them to function and to hold their walls in contact, during periods of rest. This vast amount of work of adaptability over centuries carefully adjusted to furnish support and meet resistance and yet allow easy passage to functioning tubes would seem too strong an argument against the advocate of prolapse theory, who think of rectum alone without any thought or consideration for the pelvic floor.

Considerable difference of opinion exists as regards pathological classification and treatment of prolapse of the rectum. One surgeon

A paper read at the 55th meeting of the G S Medical College and K E M Hospital Staff Society, Bombay, on December 8 1945 with Dr V M Kalkind in the chair

may recommend local or non-surgical treatment while another may suggest some type of intra-abdominal operation. In an attempt to co-relate and classify the basic pathological physiology and various methods of treatment for this condition Rankin of the Mayo-Clinic has suggested the following classification

- 1 Prolapse of the rectal mucous membrane alone
- 2 Prolapse of rectum proper (Procedentia)
- 3 Intussusception of the recto-sigmoid

A detailed description and discussion of etiology symptoms and treatment of these three types is not possible tonight because of the short time at our disposal. So I shall restrict my remarks to the second group, namely, the prolapse of the rectum proper

This is characterised by the presence of all coats of the rectum in the protrusion. This is a true prolapse and is almost always met with in adults

Etiology —

The rectum is held in position by several supports
 the lower portion by —Pelvic fascia—Levator-ani-muscle—Fibrous attachments to the coccyx, the prostate or vaginal walls
 The middle portion by —Loose fibrous tissue which passes from the sacrum along the lateral sacral arteries
 The Upper Portion by —Various peritoneal folds

During the production of complete prolapse these various supports undergo some weakening or destruction and some force dislodging the organ from its position is exerted. At times some congenital abnormality exists, such as an abnormally deep cul-de-sac. In general if some anatomical weakness or abnormality is present any exciting cause may initiate the prolapse

The etiological view of most recent authors is that the rectal prolapse is a sliding median perineal hernia, through the pelvic fascia. This was first propounded by Moschowitz in America in 1912. After careful anatomic studies he stated that the prolapse of the rectum is a hernia in all its features. It confirms all the recognised principles of hernia in other parts of the body. He reminds us that

- a The entire abdominal parietes are lined by the peritonium
- b External to the peritonium there is everywhere a layer of fascia with different names in different parts of the body such as Transversalis fascia, Pelvic fascia, Iliac fascia, Diaphragmatic fascia, etc., The entire fascia is a continuous layer
- c All large blood vessels and the viscera of the abdomen lie on the fascia and are covered by the peritonium

Hernia occurs only at places where blood vessels and viscera make their exit. In other words these weak anatomic points must be attenuated perivascular or perivisceral projection of the fascia. Two fundamental anatomical facts should be borne in mind in considering the problem of prolapse of the rectum namely that the peritonium covering the anterior surface of the rectum is intimately adherent to it and that the upper surface of levator-ani is covered

with dense fascia. Normally this fascia together with other component parts of the perineal body prevent the progress of hernia in a downward direction for a time.

According to Moschowitz the production of prolapse is as follows —

The peritonium at the bottom of the pouch of Douglas is driven downwards by increased intra-abdominal pressure through a defect in the pelvic fascia at the site where rectum emerges from the abdominal cavity. Here the resistance offered by the perineal body prevents further downward progress of the hernia and its direction is thus diverted posteriorly on to the anterior wall of the rectum, which gives way to produce pouching of this wall. As the hernia proceeds, resistance is met with posteriorly by sacrum and coccyx, and the course is again changed, at first in downward and forward direction and finally backward through the anus. The prolapse therefore involves the anterior wall of the rectum first and as it enlarges, it draws in the two lateral walls and finally the posterior wall, until further drawing of the bowel wall is prevented by the firm fixation of the organ.

In the fully developed prolapse the opening of the bowel should be placed posteriorly as more of the anterior wall takes part in the sliding process. After reduction of the prolapse, if a finger is pressed on the anterior wall of the rectum, it is prevented from coming down even on straining. This clinical test again confirms the theory of the sliding hernia of the anterior wall of the rectum. In all our cases we could testify to the validity of this clinical sign. However we did not observe the posterior situation of the bowel opening in the fully developed prolapse in all our cases.

If the above conclusions are correct then the only treatment should be removal of the sac and repair of the anatomical defect in the pelvic fascia.

Signs and Symptoms — Chief symptom is the protrusion of the mass from the anus. It occurs in both the sexes. In our small series all the patients were males. It has been mentioned in the text books that this condition is usually associated with pre-existing pathological condition in the rectum. It is usually secondary to some type of disturbance which causes excessive straining at stool. Locally piles, prolapse, stricture, atrophic or paralytic sphincters are the most common pre-disposing conditions. At times diseases of the neighbouring organs such as an enlarged prostate is met with. Again it has been mentioned that the disease is met with in patients of advanced age, suffering from some debilitating maladies. All our patients were young. The age varied from 20 to 35, average being 26. One patient was mentally defective and at the time of admission was suffering from severe anaemia—The blood count was just over 15 millions. The other five patients were all healthy individuals.

One of them suffered from constipation, and in the rest, history of dysentery or history of frequency of stools with blood and mucus,

was present either at the beginning of the trouble or sometime during the progress of the condition. The prolapse was present for 2 to 10 years before the patient came under observation—average duration being $6\frac{1}{2}$ years. The onset in all was gradual. It was easily reducible at the beginning, but at times during periods of diarrhoea or excessive straining, it had come down suddenly and was difficult to replace. In one patient, general anaesthesia had to be given to achieve reduction.

The length of the prolapse varied from 3 to 6 inches. In none of our patients were we able to detect the presence of coils of intestine in the anterior part of the mass, while under observation. In two patients the sphincters were lax and they suffered from constant disagreeable secretion of mucus. None of our patients complained of pain, but all of them had a sense of constant discomfort in the rectum. No pathological condition such as piles, polyp were present locally in our cases. The mucous-membrane of the rectum was oedematous in all, but in only one case there were two superficial ulcerations. Blood stained discharge per rectum was present only in the case of mentally defective. Inquiry is being made whether such condition of prolapse is more common amongst the inmates of the mental asylum. The occupation of the patients were varied. One patient was a milkman, another a mill hand, 3rd, a chauffeur, 4th a silversmith and 5th patient was a tailor.

Diagnosis The diagnosis of proctodentia is not difficult and I shall not go into details of this.

Treatment may be non-surgical or surgical. The non-surgical treatment is of use only in early cases when protrusion is small. This consists of

- 1 Application of soothing lotions to relieve the irritating mucous membrane
- 2 Submucous injections of astringents like alcohol, ergot, etc
- 3 Mechanical supports

All these are obviously palliative. Once the prolapse is big as in all our cases, only treatment is surgical.

In main five different types of operations are carried out for such condition —

- 1 That which causes the narrowing of the anus and the rectum
- 2 That which restores the pelvic floor by suturing the levator-ani or glutei together
- 3 That which suspends or fixes the prolapsed bowel
- 4 That in which the prolapsed bowel is resected
- 5 That which is designed to obliterate the pelvic cul-de-sac and repair the defect in the pelvic fascia

I shall now discuss these different methods —

- 1 This can be achieved by removal of "V" from the posterior portion of rectum and anus. Destruction of mucus membrane by cautery or removal of strips of mucus membrane and placating the wall longitudinally will produce narrowing of the lower portion of the rectum. Similarly injection of paraffin subcutaneously or

introduction of silver wire round about anus will narrow that orifice. These procedures will only be successful in the initial stage of prolapse. Pemberton is of opinion that weakened or paralytic sphincter is not the cause of rectal prolapse. This may produce incontinence but not prolapse. He suggests that the rectum with adhesions in the pelvis is like a prisoner in chains. The external sphincter is compared to the prison door. Even if the prison door is open the prisoner in chains cannot come out, but without the chains it is likely that he may break open the door and escape. Similarly as long as the rectum is held up with adhesions or ligaments in the pelvis no prolapse would occur, even if the sphincters were loose, but once the support of the rectum gives way, it will protrude through a normal sphincter. In early cases these types of operations may be successful but in the massive type recurrences have been more common.

2. Objections to these operations done on the perineum is that it is not possible to repair, the defect in the pelvic fascia with requisite care and exactness through the limited space. Again levator-ani are not the chief support of the rectum. While doing the perineal resection of the rectum, one finds how difficult it is to bring down the rectum after cutting the levator-ani alone and only after severing the lateral ligaments of the rectum, it is possible to bring out the lower end of the bowel.

3. Rectopexy, Sigmoidopexy or Rectosigmoidopexy as suggested by Pemberton are the operations which fall in this group.

Lockbert-Munumary's operation pays attention to the posterior wall of the rectum only, which does not take part in the descent primarily. In a recent article this author has suggested that in case the anterior wall is found to be involved a similar operation can be carried out anteriorly. Objection to these types of operations is that no direct attack is made on the fascial defect.

Pemberton advocates Recto-sigmoidopexy, not that he does not believe in the theory of Moschowitz, but he is definitely of the opinion that the most important predisposing factors in the development of the prolapse, are the abnormally loose attachments of the rectum and that the prolapse would not occur, if the bowel is firmly fixed. In cases of inguinal colostomy if the proximal loop of the bowel is slack, prolapse through the colostomy opening takes place. That is why one prefers the descending colon which is devoid of the mesentery and is fairly fixed. If the proximal loop has a loose mesentery, we pull out more of it and only fix the bowel when we find that the slack has already been taken up. Pemberton separates the rectum from the hollow of the sacrum and after pulling it up sutures the sigmoid to the psoas muscle as is done in sigmoidopexy operations. In this operation no attention is given to the deep peritoneal pouch and the defect in the fascia. Through this a perineal hernia may occur subsequently even without a prolapse.

4. Resection of the prolapsed portion of the bowel will not correct the defect in the pelvic fascia. Only dangers of these

ten months ago All these patients are very happy about the result Graham's operation is done by other surgical units also in his Hospital In fact Dr Munsif did the 1st Graham's operation in this Hospital more than 2 years ago

Conclusions—The treatment is based upon one's conception of the condition If the treatment of prolapse is and always has been directed to the bowel pathology the pelvic floor will be overlooked If the condition is a herniation the peritoneal pouch and the pelvic fascia will receive joint consideration We have taken the later view Our series is small to make all inclusive assertions, but we do suggest that our small experience indicates that the method is worthy of further trial, before an accurate evaluation can be attained We realise that the success or failure of any method cannot be properly judged until a large group of patients have studied over a prolonged period However in view of poor results obtained in advance cases of prolapse of rectum when other operations have been done and because of the theoretic soundness of the operation and highly gratifying results of this distressing condition from the patient's point of view we are encouraged to present it for consideration

DISCUSSION

Dr K. G. Munsif reported two cases of Prolapse of Rectum The first case a man aged 40 years having a recurring prolapse of 4 years, duration The prolapse was reduced previously by various methods and at the time of admission it had become irreducible Graham's operation was done on him on 2-7-43 and after an uneventful recovery was discharged 15 days later The second case a female aged 40 years had prolapse of rectum of 5 months duration with severe anaemia Graham's operation was done The result in both these cases was gratifying

Lt Col. Bond divided cases of prolapse in two types in which there were Atonic sphincters and 2) where the sphincters showed some tone He was of the opinion that it was not worth while treating the first type until the muscle tone was regained Electrical faradist stimulation was necessary at first because he patient could not voluntarily contract the muscles followed later by sphincter exercises In his opinion good results were obtained by combination of operation as for example Mummery with Moschowitz and temporary colostomy He added that Fascia operation without stripping the Peritoneum was a simpler operation where the Peritoneum is stitched over the Fascial strips and anchored to the bony pelvis

Dr S. B. Gadgil said that the speaker had not dealt with prolapse of the rectum in children, where treatment to improve the general health and other associated conditions like whooping cough, gave satisfactory results without having recourse to operation In adults in his opinion though there was a weakness of the sphincters, this may not be the cause of prolapse He further added that in every operation for prolapse, the principle followed in the treatment for prolapse of the uterus might be observed, fixation of the uterus and repair of the perineum He further observed that Lockhart Mummery's operation if carefully followed, gave good results He then described the technique of the operation in detail and also one to fill up the pouch of Douglas the latter could be performed by opening the abdomen in the iliac region pulling the prolapsed gut and packing the cavity with strips of gauze the edges coming out of the abdomen He further said that these strips were to be removed gradually in a fortnight the cavity being filled with granulation tissue and occluding the space between the bladder and the rectum

Dr A. V. Balligal said that Graham's operation had brought hope to a hitherto disappointing chapter in operative treatment of massive prolapse He described two operations carried out by him on males between the ages of 20 and 30 years with good results He further added that medical borders of the levator ani could be recognised with great difficulty as the muscles were attenuated The operations required patience and involved a tedious technique but the results were satisfactory

Dr G. S. Worah wanted to know whether the deep peritoneal pouch was seen in the recto vesical reflection as occurred in cases of Hernia He added that Graham's operation as all Hiernal repair operations would fail occasionally and therefore suggested that a recto-sigmoidectomy was preferable as the herniated part was removed

Dr R. G. Glude said, For the period extending from July 1936 to November 1945 there were 8 cases in his unit Of these three were cases of Massive Prolapse of the rectum all in males between the ages of 45 and 56 The first case refused an operation The second was extremely anæmic, debilitated and debilitated After treating his general condition Graham's operation was performed on him but the wound ruptured partially necessitating secondary suture a month later His general condition deteriorated the patient succumbing 5 weeks after the operation The third case was of Massive Prolapse of 6 years duration with frequency of stools without diarrhoea Recto-sigmoidectomy with suturing of the levator ani below Douglas's pouch as suggested by Cohn was done (Am J Surg 44-42) He had an uneventful convalescence and to date there is no stricture and no prolapse and the patient has a good control over defecation

Dr M. M. Pandya said that in 4 cases which he performed Recto-sigmoidectomy only one case developed a stricture which had subsequently to be dilated He suggested that a comparative study of the two operations might be done for the proper evaluation of results

Dr J C Patel said that in Chronic amoebiasis, straining at stools occurred due to a feeling that the rectum was not properly evacuated. He suggested an examination of stools in these cases as well as in those where diarrhoea was a symptom.

Dr S H Chitnis asserted that in all the cases mentioned by Dr Phadke the stools were examined and treatment for amoebiasis carried out.

Dr B N Purandare said that in his experience he had not encountered a single case of prolapse of rectum in women. This low incidence in Indian women was remarkable in spite of the fact that damage to the anal sphincters was common in parous women. He was of the opinion that the factors favouring rectal prolapse in men probably led to the development of enterocele in the female.

Dr A. E. de Sa said that he would confine himself to rectal prolapse as seen in children. He classified prolapse in children roughly into two big groups. The first included the healthy well nourished children of the middle and upper classes in whom the prolapse was entirely the result of perverse habits at defaecation such as abstaining from a stool when the natural desire was felt. In this group of cases no operative treatment was necessary. The discipline of a Hospital or a Nursing Home which ensured regular habits—if maintained over a period of two or three weeks, generally resulted in a cure, unless the child on going home, returned to its old habits.

The second group comprised the wasted underfed children of the poorer classes in whom the prolapse was the result of loss of the perirectal fat and atony of the musculature of the pelvic floor. These children needed more than the discipline of a Hospital or a Nursing Home to effect a cure. Some form of operative treatment was essential. Where linear cauterisation of the mucosa was performed the speaker made it a practice to carry the cauterisation down to the perianal skin. The pain resulting from the perianal burn ensured a more or less continuous contraction of the sphincter and.

With regard to sphincteric exercises he had found that the simplest way to ensure sphincteric contraction in children was to stimulate the perianal region with a pin. It was a simple and more economical method than faradism applied to the sphincter and.

Dr Phadke in reply, did not agree with Col. Bond about the lax sphincters. He did not think that the lax sphincters were responsible for the prolapse. This has been upheld by many proctologists and Gynaecologists who have the common experience of seeing cases of extensive perineal tear without any suggestion of prolapse of the rectum. Mere strengthening the sphincters by stimulation with some electric current or active exercises was not going to cure the prolapse.

In reply to Dr Gadgil he referred to the views expressed in his paper about the importance of the sphincters and the unscientific basis of Lockhart Mummery's operation. He thought that the method of packing the pelvis with gauze and removing it again after a few days in order to establish adhesions in the pelvis to prevent any more prolapse was a very crude method and could not be entirely relied upon. Besides the incidental complications would certainly arise such as internal strangulation and incisional hernia.

Dr Phadke agreed entirely with the views expressed by Dr Baliga, Dr Pandya, Dr Glinde and Dr Worah who had carried out 'recto-sigmoidectomy' operation in some of their patients with satisfactory results, as long as they had been able to follow them up. The speaker had already given his objections to this type of operation but he did not want to be dogmatic at that stage. Whatever were the merits of the other operations he believed in the theoretical soundness of Graham's operation and had decided to carry this out in his unit. He intended to carry on this procedure for the next few years and then judge the results. In reply to Dr Worah he said that the pouch or the sac seen from the abdominal aspect was like a sac of any direct hernia, but deeper. The two previous operations done on the patients he mentioned in his paper were (1) Duplications of the lower end of the rectum (Rehn Delorme operation) and (2) Lockhart Mummery's operation.

He agreed with the suggestion put forward by Dr J C Patel that diarrhoea rather than constipation was responsible for prolapse, and in all the cases mentioned stools were examined and in three of them treatment was given for amoebic dysentery without any benefit.

He thanked Dr B N Purandare for supporting his contention that lax or torn sphincters did not produce prolapse.

Critical Notes and Abstracts

EXPERIMENTAL INVESTIGATION OF BURASAINÉ IN THE TREATMENT OF MALARIA (S Davidson—East African Med J 1945, Mar, V 22 No 3, 80-85)

The author reports the treatment with burasainé of 15 non-immune and 3 immune Africans suffering from *P falciparum* malaria. Burasainé comes from Madagascar. It is the total alcohol extract of the root of a tree, *Burasainé madagascariensis* Thouars (family Menispermaceae). The extract contains alkaloids with the methyl-orthoquinino-isoquinoleic ring such as is found in hydrastine and berberine. The extract was made up into tablets of 5 grains each. Sixteen tablets were given in 24 hours. Swallowing the tablets with water often caused nausea and vomiting, so each dose of 4 tablets was dissolved in 2 ounces of glucose water, and 10 minims of dilute hydrochloric acid were given. No toxic effects, except vomiting, were noted. Three non-immune control cases were treated with quinine. All but one of the patients treated with burasainé only, left hospital free from fever and parasites in the peripheral blood. The resistant case was given quinine on the 19th day and recovered. Burasainé acts very much more slowly than quinine, though from the data supplied it is not possible to make any exact comparison of the efficacy of the two drugs. It would seem that burasainé has some definite anti-malarial properties.

CH'ANG SHAN A NEW ANTI-MALARIAL DRUG

A number of Chinese workers (C S Jang, F Y Fu, C Y Wang, K C Huang, G Lu, and T C Chou), of the Pharmaceutical Laboratory, National Institute of Health, Chungking, have reported in 'Science' (January 11, 1946) of their investigations on the anti-malarial action of *Dichroa febrifuga* of the family Saxifragaceae. The shrub, commonly known as 'Ch'ang Shan', grows in China, and its roots have long been used there as a malarial remedy. It is also found in north-eastern India, Java and the Philippine Islands.

Mr C S Jang and his collaborators extracted from Ch'ang Shan and also from another Chinese herb, Shah chi, four crystalline substances: Dichrin A (m.p. 228-230°C) and Dichrin B (m.p. 179-181°C) and Dichroine A (melting at 230°C with decomposition) and Dichroine B (melting at 237-238°C with decomposition). The former two are neutral principles and the latter two are alkaloids.

A solid extract of the herb, in a dose of 0.03-0.06 equivalent to about 7.5-15.0 gm of the crude drug, was administered by mouth twice or three times daily for an average of five days on 13 clinical cases of tertian malaria. The drug was found to be as prompt as quinine in controlling the fever, although its anti-parasitic effect in converting positive smears into negative was slightly slower.

Animal experiments also demonstrated the anti-pyretic and anti-parasitic effects of Ch'ang Shan. A simple decoction of the crude drug controlled the febrile temperature of rabbits inoculated with

B Coli vaccine In another experiment malaria was induced in chicks infected with *Plasmodium gallinaceum* and Ch'ang Shan was given by stomach tube twice a day for 1 to 7 days in dose of 1 gm/kgm. The drug controlled the infection which would have otherwise proved fatal.

Pen Ts'ao Kang Mu, the Chinese Book of Herbs, describes Ch'ang Shan as a poisonous herb. The authors found that the toxic effects of the drug were none more serious than nausea and vomiting. In dogs, fatal doses of the drug, however, produced intense congestion and haemorrhagic patches throughout the gastro-intestinal tract, but no specific lesions were found in the liver, spleen, and kidneys.

It is of interest to note that the anti-malarial action of this drug was also known to Indian physicians for a long time. Dr David Hooper, writing in 'Nature', recently recalls that fifty years ago, when he was in India, an Indian physician sent to him 'some stems of the plant as fever remedy and suggested that it might contain an alkaloid similar to quinine'.

Book Reviews & Notices

THE 1945 YEAR BOOK OF PEDIATRICS edited by I. A. Abt and A. F. Abt. Chicago. The Year Book Publishers, 1946. Pp 448. Price \$ 3.00.

The speciality of Pediatrics is rapidly being established in India. Many cities have hospitals for children only or special children's wards attached to general hospitals. Many physicians are confining their practice to children only and the universities and the College of Physicians and Surgeons have instituted a special diploma in Child Health. To the student, the pediatric specialist and the general physician interested in children, no book can be more welcome than this annual review of the year's pediatric literature. The articles are well chosen, critically abstracted and presented in an agreeable form. The value of sulphadiazine in controlling the spread of meningococcal meningitis appears to be now well-established and it may be safely used as prophylaxis in schools or in any limited group. The use of neostigmine methylsulphate to relieve spasm of the muscles in anterior poliomyelitis is suggested. The role of allergy in acute abdominal pain is stressed. The use of ethylene disulphonate in children's allergies appears to be valueless.

DIETETICS IN GENERAL PRACTICE by J. R. Goyal, Delhi. The author. 2nd edition, 1946. Pp 462. Price Rs 8/.

This second edition is fully revised and enlarged. The latest additions to the knowledge on the subject likely to be of use to the general practitioner are incorporated and new chapters on foreign and Indian dietaries added. Vernacular names of many food stuffs are given. This new edition will be as appreciated by the general practitioners as the first one.

Reflections and Aphorisms

TREATMENT OF ESSENTIAL HYPERTENSION

"Let us take the example of a middle-aged man refused by a life insurance company because of high blood pressure. His physician rules out glomerulonephritis and decides that the patient is suffering from essential hypertension. Then, all too frequently, attention is concentrated on the effort to "bring the blood pressure down." The patient demands to know the blood pressure figures, on each visit to the physician he waits with anxious concern to hear the latest reading and frequently has ideas of a "stroke", "heart failure" or "Bright's disease" in the back of his mind.

"Just what has been done to this poor patient in the effort to "bring his blood pressure down"? Because of an ill-founded idea that protein is responsible for hypertension and kidney disease he is denied meat and eggs, especially red meat, which for some reason is looked upon with particular dread. Then his diet is rendered even more unpalatable by the withdrawal of salt. One would sympathize with this half-starved victim of good intentions except that he probably would not be able to eat anyway, his teeth having been removed on the theory that focal infection has something to do with hypertension. Even before this period he has sacrificed his tonsils and has had his sinuses punctured because of the same theory. In case he actually had been able to eat some solid food, in spite of these previous therapeutic measures, the slight colonic residue was promptly washed out by numerous "colonic irrigations," especially during the period when the theory of auto-intoxication was enjoying a wave of popularity. To add to his unhappiness he may be told to stop work and exercise, and, of course, is denied alcohol and tobacco as well as coffee and tea. And now to cap the climax of his difficulties, the unfortunate person with hypertension seems about to fall into the clutches of the neurosurgeon, who is prepared to separate him from his sympathetic nervous system.

"One of the greatest faults in the management of hypertension in this country has been the emphasis on "bringing the blood pressure down." We must look upon the blood pressure curve in the same way that we do the fever curve in an acute infectious disease and realize that it is just as wrong to fasten our attention on bringing the blood pressure down without understanding and treating the individual who has the blood pressure as to concentrate on reducing the fever. We have paid altogether too much attention to physical measurements in hypertensive disease. While it is undeniably true that the size of the heart as determined by the x-ray, the height of the blood pressure as determined by the sphygmomanometer, the condition of the retinal vessels as determined by the ophthalmoscope, and the state of renal function as determined by the various clinicopathologic tests are all absolutely essential to the understanding of the hypertensive individual, they are only the beginning and not the end of the study. We must try to understand the total personality of the individual who has hypertension or who seems destined to develop it. It is the study of emotional factors which may provide us with the key to the successful management of the hypertensive individual."

—EDWARD WEISS

"A DOCTOR AND HIS BOOKS"

V R KHANOLKAR

शब्द थोडे अर्थ फार ।

कृपा करुनी याचा अर्थ विचार । करावा सर्ती ॥

वामन पंडित (निगम सार) श १५९५

I am happy to be here on this occasion, because it is good to meet people who are outside the circle of one's daily work, and to associate with colleagues who are keen on an advancement of learning. Your association intends starting a medical library. I am glad to have been asked to open it. I have a fondness for books, and I rejoice to meet others who have the same leanings. My earliest memories go back to a small room stacked to the ceiling with books and the privilege of being allowed to sit huddled besides my father on cold wintry mornings, while he pored over some rare manuscript on ancient philosophy, before starting on a round of visits to his patients. Many years have rolled by and I have been led to follow his footsteps. Although I have not amassed riches, I have discovered a never failing source of strength, in these days of doubt and uncertainty, in the books that line the walls of my own room. If I tell you my views about a library, the way it should serve the medical community and the general public in your locality, it is because I have had an opportunity of visiting libraries in different parts of the world and also because I have given this matter much thought and some inquiry.

A library is a place set apart to contain books, for reference, reading or study. What has a medical man to do with such a place? You are a practical people, and you might say that you have no truck with books, that the only book you read is the book of nature and that you consult only your own experience. This is false doctrine. There is no class of people who stand in greater need of books and journals than medical practitioners unattached to a hospital, and unstimulated by the enquiring minds of young students. "For the general practitioner a well used library is one of the correctives of the premature senility which is so apt to overtake him. Self-centred, self-taught he leads a solitary life and unless his everyday experience is controlled by careful reading, or the attrition of a medical society, it soon ceases to be of the slightest value and becomes a mere accretion of isolated facts without correlation. It is astonishing with how little reading a doctor can practise medicine."

A lecture delivered at Poona to the members of the Indian Medical Association on 27th January, 1946

but it is not astonishing how badly he may do it"² The spun out prescriptions, opinionated assertions and the studied absence from clinical or scientific meetings of many successful members of our profession bear testimony to the essential correctness of the above statement

I should like to start by correcting two mistaken opinions about books, which are often expressed by well meaning but ignorant people It is said that books contain mainly obsolete ideas, which are inapplicable to current problems in medicine It is true that advances in technique and improvements in specialities have been prodigious during the last fifty years It is however, surprising that the observations and the shrewd interpretations of an Addison, Bright or Laennec remain as instructive to-day as they were a couple of hundred years ago The impressions which many of you may be carrying over from undergraduate days are unfortunate While you were haunted by the spectre of examinations, your books often brought weariness and vexation Now that you have laid aside the absurdities of our examinations, you would discover in your books the visage of a friend, if you gave them a chance to get acquainted with you

It is sometimes suggested that books could not possibly comprehend the living phenomena which have become our personal experience Nothing could be further from the truth. Good books probe the events of life with penetration and perspicacity beyond the powers of most of us The capacity for making accurate observations and realising their significance depends on an enrichment of our limited knowledge with the experience of others "Every physician will make and ought to make observations from his own experience, but he will be able to make a much better judgment and juster observations by comparing what he reads and what he sees together"² You are probably familiar with the oft-repeated saying of Osler "To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all"

Books are more than a means for improving our knowledge and sharpening our sensibility, they are a contribution and a part of the restless life round us A good library is therefore much more than a place set apart for books It has recently been described as "a storehouse of old knowledge and a powerhouse for new knowledge" A wisely run medical library imparts education, enables research and promotes culture in a community which uses it intelligently I would deal with these functions at some length because it is at the bedside, the laboratory and the library that modern medicine is being insensibly forged into what we are proud to call a science of medicine

Education has three ends—vocation, citizenship and living Sound medical education should therefore consist of three distinct types of training, viz vocational, social and theoretical Our medical schools and colleges have concentrated above all on the first type and have neglected the last two, either from poverty of outlook or from actual design The academicians have busied themselves with syllabuses, regulations and restrictions They have not borne in

mind the wise observation of Gibbon, that "the power of instruction is seldom of much efficacy, except in those happy dispositions where it is almost superfluous" These three types of training should run concurrently during the medical curriculum and throughout the life of a medical practitioner The vocational education alone is capable of turning out technicians—remarkable technicians—but never accomplished physicians It is planned for giving a sound factual knowledge of morbid processes and for imparting technical skill in diagnostic and therapeutic procedures It could be acquired with little aptitude and much repetitive exercise Most of us have admired the ease and dexterity with which some technicians administer injections and medical assistants extract teeth and cataracts

The role of social medicine is but vaguely understood in most countries It will probably assume the most important place in our future training and we are beginning to get just an inkling of its extent from some European and American schools Its function has been explained by one of its most able exponents as follows "Social medicine means what it says It embodies the idea of medicine applied to the service of man as *socius*, as fellow or comrade, with a view to a better understanding and more durable assistance of all his main and contributory troubles which are inimical to active health and not merely to removing or alleviating a present pathology It embodies also the idea of medicine applied in the service of *societas*, or the community of men, with a view to lowering the incidence of all preventable disease and raising the general level of human fitness"⁶

The third type of training is theoretical, which evokes "a fondness, or more exceptionally a passion, for understanding, and through this achieves conscious independence of thought and judgment"¹ This type of training is needed to day more than ever before It is our only defence against the rising flood of salesmanship, and the ill-informed opinions in newsprint and on the air which invade the innermost recesses of our homes A medical man has to weld himself an armour for protection, 'In a world where a disquieting proportion of what is offered him in conversation and in the generality of journals and books is inaccurate, slovenly and redundant'¹ Throughout the period of our training we are assailed by the clamour of specialists for a mass of detail, and the insistence of academicians on a passing acquaintance with a wide variety of subjects Recently MacCracken the president of Vassar has protested against this flutter and turmoil regarding educational programmes The following would bear careful reflection "Where there is poor teaching and mediocre living you will find the professors clamouring for compulsion to make their students come back to their courses Strange as it may seem, students recognise good teaching when they see it The real problem is not how to regulate the student some more, but how to set him free, how to give him the four freedoms of college freedom from family, freedom from faculty, freedom from administration, and freedom from himself The success of education depends on the consent, interest, participation and integrity of the educated" We must keep our curiosity wide awake, to escape getting 'ed

within the narrow limits of a small speciality We must also try to acquire a profound knowledge of a particular branch of study which we may have made our particular interest "Let us try to find out what Nature has planted in us of the best, what she intended to do with us and profit by it Do not let habit, fancy, distraction or caprice wrap us up in a lot of superfluities, or rig us up in the parti-coloured cloak of a harlequin" (a)

I think I am right in saying that for the generality of our profession the libraries are probably the only source of post-graduate education Books and journals furnish them with the experience of their more fortunately placed colleagues They bring recommendations born of experience in better equipped institutions, and warnings based on failures Unaided by such education the general practitioner settles down into a condition so elegantly described by Roustan "A medical man of this type is insensible to the infinite variety of disease For him there exist a small number of labels—like those seen dangling at the foot of hospital beds Each of these 'disease entitles', as they are called in his jargon calls for a treatment which if it eludes his memory is readily looked up in a book of prescriptions or a compendium of symptoms" (b)

The second function of a medical library should be that it enables research It is unfortunate that the word "research" has gained wide currency during recent years It is amusing to listen to politicians, administrators, educationists and businessmen waxing sentimental over it, as they roll it about in their official utterances Research is not a magic word, it is certainly not a slogan It is "an investigation directed to the discovery of some facts by careful study of a subject" Such study has paid huge dividends in recent years and has therefore enamoured many people

It has been noticed that "a purely teaching institution, wherein no one is engaged in the forging of new knowledge, or in thinking on broad lines about the problems of medicine is a dead school" I may be permitted to add that any community of medical men which is concerned with an unthinking prosecution of their profession is a dead community, and differs intellectually in no recognisable manner from a congregation of quacks

It is necessary to review some popular notions about research before we consider its application to our work. It is believed by some people that research happens in places where there is complicated apparatus, glistening glassware and a host of technicians "going through the movements of doing research"⁵ Nothing could be more deceptive, all these appurtenances may or may not assist the functionings of an original mind Without his guidance the test tubes, the flasks, the microscopes and the vacuum pumps are reduc-

⁵ Note.—The translations are not literal The original text is therefore printed in the footnotes

(a) Das ist nun was aus den Menschen werden kann eigentlich hangt soviel Unnutzes um unsern aus Gewohnheit, Neigung Zerstreuung und Willkur ein Lumpenmantel zusammen gespettelt Was die Natur mit uns gewollt, das Verzuglichste was sie uns gelegt, konnen wir deshalb weder nuffinden noch ausuben Goethe —Wilhelm Meisters Wanderjahre Leipzig Insel Ausgabe p 897

(b) Aux yeux d'un tel medecin l'infinie diversite des malades ne compte plus il n'existe qu'un nombre limite de ces etiquettes qu'on suspend aux lits d'hopitaux et chacune de ces "enlites morbides" comme il dit en son jargon commande un traitement que peut indiquer le manuel ou le formulaire si la memoire reste en default D Roustan —La culture au cours de la vie Paris 1930 p 16

ed to junk, collecting cobwebs during the passage of sterile years. There is another body of people who cherish the belief that discoveries gush out from people like the Ganges from the chevelure of Shiva. It is difficult to eradicate this belief, although past experience has shown that inspiration comes to those alone, who are prepared to receive new ideas after much labour, study and reflection. Research aims at a discovery of new facts and a revision of accepted ideas in the light of newly discovered facts. It has to rely on an acquaintance with a body of valid ideas about the subject under investigation. It can, therefore, be undertaken by those who have been trained in the application of scientific method to observed phenomena, and have acquired an ability to deduce logical conclusions from them. It can only be guided by those who are not only trained in the intricacies of the necessary techniques, but who have also a flair for original thinking, a passion for pursuing new knowledge and an ability for grasping the significance of a discovery when it unfolds before them. There is one other misconception, that a person who publishes five papers in a year does more research than another who publishes one paper in five years. This is a harmful belief. Nearly three hundred years ago John Mayow wrote, "Disease as it stalks through the land cannot keep pace with the incurable vice of scribbling about it." This sagacious observation is more significant to-day than it was in his time.

It might be argued that research is not the concern of general practitioners. This is erroneous. Research is a concern of everyone who is prepared to make a reasoned use of his senses, who has an urge to explore problems which confront him in the course of his daily work, and who has the reflective bent of mind which is unsatisfied with the current conception of things. I need not remind you that Jenner, Koch and Mackenzie were private practitioners when they laid the foundations of their startling discoveries. I may also add, that in truth, material considerations might have delayed, but did not deter, these men from undertaking research. There is however, one necessary condition before embarking on any investigation. No research worker is entitled to advance what he may believe to be a new idea or to commence a study to explore it, without knowing what other people have achieved on similar lines before him. It is necessary to avoid a waste of human effort, it is also imperative to verify conclusions based on insufficient knowledge.

And now we will consider the third and to my mind the most interesting function of a library. A library promotes culture among its intelligent users. A chemist, a physicist, an engineer or an architect deal indirectly with that which motivates human action or regulates life processes. "Science without humanism may work with atoms, but it will not work with men." The physician is concerned with the well-being of living persons all the time. He does not work in the seclusion of a laboratory or the din of a workshop. He has to adjust his theory to the feelings, emotions, faults and weaknesses of his patients. He has to develop a humane outlook, finer sensibility and reassuring personality. More than all else, he has to acquire an understanding of the people among whom

works All the great men of our profession were not only possessed of wide knowledge but also deep understanding We could say that they were cultured physicians Let us, therefore, look into the nature of this culture, concerning which there are so many bickerings in our country Culture is an enlightenment or refinement of taste acquired by intellectual or aesthetic training "The idea expressed by the Greeks by *paidea*, the Romans by *humanitas* is imperfectly expressed by the more artificial word culture" Culture is a way of looking at all things philosophically, of lifting oneself out of detail, without being estranged from one's surroundings"(c) I believe that the crux of the idea lies in acquiring a philosophical frame of mind without becoming a stranger to one's own people If we apply this criterion to ourselves, the extent to which we would be found wanting would surprise us Twenty-five hundred years ago our people understood what their doctors were doing The medical men talked the same language, thought the same thoughts and acted on the same assumptions as those among whom they worked The philosophical ideas and religious traditions were as ingrained in the healer as in the healed, and they did not appear to be working at cross purposes all the time The learned and the uninformed shared the same general outlook towards man and nature, life and death In the eyes of the people, the physician was a cultured man who practised the healing art in the same manner in which the gods dispensed justice and happiness This unification of ideas resulted in a remarkable material and spiritual advancement of our people Three centuries before the Christian era, Ashoka organised medical relief throughout his vast empire He ordered places to be built in the town and country, for the care of rich and poor, for men and animals³ The people studied and practised the science of longevity (Ayurveda), and the tenets of its teachings permeated all levels of society They continue to influence our thinking even to day, and appear to offer the most natural explanation of disease and the most plausible way of dealing with it When the Europeans came to our shores some 400 years ago, they were accompanied by a few physicians, some of whom gained considerable influence over the blase, degenerate rulers of the provinces We now know that their medicine was in no way superior to the systems prevalent in this country, either in theory or in practice Their practitioners, however, were men of integrity and devoted to their own way of life

During the last two hundred years the technical and theoretical advance of the physical sciences has been phenomenal Medicine has sometimes outstripped and at others followed in the wake of fundamental discoveries in the natural sciences The progress of Western Medicine has been coeval with social improvements and educational advancement of their people A vast majority have maintained their faith in the efforts of their doctors, and the educated people in those countries have kept track of the great discoveries in medical sciences "Men do not willingly accept that in which they do not believe In ordering of their lives, and even in the regulation

(c) La culture est l'habitude d'envisager philosophiquement les choses de s'élever au-dessus du détail de ne pas se trouver dépayse dans le temps ou l'on vit Alfred Croiset — *Libres entretiens de l'Union pour la Vérité* Be serle 1011 12 p 138

of their vices and the reform of their shortcomings, men and women are far more willing to seek the advice and help of the medical man than once they were. The reason is, without doubt, that his advice is much more worth having than it once was. The shifting of men's trust implies a shifting in their faith" 4

And now let us see how we in India have reacted to the influx of new knowledge. We have acquired it in a foreign language, we have practised it in unfamiliar ways, we have never attempted to explain to our own people the reasons for doing things in the way we have been doing them. In fact we have lost the faculty of doing so. We have tried to cash in on the oddity of our proceedings, the Lethean atmosphere of our operating rooms, our glittering appliances and our archaic phraseology. We have endeavoured to mystify rather than to enlighten our people. Is it small wonder then, that we have been looked upon as the officiating members of a foreign cult, to whom people resort when other faiths have not availed, and from which they strain to escape at the earliest opportunity. We have created a situation for ourselves analogous to that caused by the introduction of a foreign body in our tissues. We have allowed an impervious wall of the giant cells of prejudice and apprehension to be erected around us, and our people have waited for an opportune moment to extrude us from the economy of our country. It is imperative, and it is urgent that we should cast aside the seclusive and esoteric attitude towards our own people and make our science their science, our philosophy their philosophy and their aspirations our own. We must learn to teach scientific medicine through our own languages and scatter far and wide such teaching. We must have faith in our science and instil that faith in the people to whom we belong.

The starting of a library is not an end in itself, it is a means towards an end. A library is intended to educate and assist the people who use it, its success therefore depends very largely on a proper selection of the books and records it contains, and the ease and accessibility of the contents to its readers. A library to be able to afford the maximum service of which it is capable should be well organised and a lot of time spent in selection and arrangement. There are excellent books and monographs which deal with the organisation of libraries and our own University arranges an efficient course for librarians under the direction of a person who is a lover of books and who knows more about them than most people. I would only add that from the very beginning you should plan to have three sections for your library. Reference books, books and journals dealing with present advances, and a section dealing with the history of medicine in your locality and in the country. There are several excellent and standard Systems of Medicine, Surgery, etc., which it is an advantage to procure for yourselves. You should also possess the *Index Medicus* and the *Annual Reviews* on different subjects which are of very great help to a busy practitioner. It should not be forgotten that reference books are for reference, and should be used as such. I think you will be well advised in not allowing your journals to leave your premises unless you possess duplicate

sets of any journal There are at present almost 2,500 medical journals which appear annually, and it will not be possible for any private organisation to subscribe for more than a score It is, however, possible to keep abreast of most of the advances by a proper selection and by securing facilities for reference by your members to larger libraries Our small group in Bombay by pooling the resources of four institutions allows our readers to have access to nearly 300 journals

It is difficult to explain to the administrators the exact function of these journals They often confuse scientific journals with current magazines which help to while away the tedium of their bureaucratic lives Scientific journals are not meant to be read from cover to cover for amusement Their main function is instruction and acquaintance with new work on different subjects If one member out of a hundred, from your association, is stimulated to undertake an original investigation after reference to a publication, the money spent by you on journals should not be considered as wasted I might suggest that in the allocation of your funds the largest appropriation should be for journals and their binding, the text books should occupy a very secondary place, particularly in view of your limited resources

The historical section appears to me the most interesting A library without it would be like a picture without a background You should therefore aim at collecting and classifying information regarding the life of our people before and since the advent of Western Medicine We should know how they lived, what were their standards of health, and their conceptions regarding ill-health. What measures were taken to prevent epidemics and what they did when they were scourged with widespread disease? The roots of our history lie deeply buried in this very city and it may be possible to collect valuable information from the lives and letters of your ancestors

Even if your library is well organised and well stocked it may still remain unprofitable if your members did not take the trouble to get acquainted with the usual bibliographical methods in their library A library as I have been trying to relate is an instrument or a tool to achieve a definite object, and man's progress has depended upon learning how to use his instruments properly I might remind you of a wise observation of the French philosopher Bergson that "if we could divest ourselves of vanity and were to restrict ourselves to historic facts and the pre-historic evidence regarding the most constant characteristic of man and his intelligence we should probably not designate our species as *Homo sapiens* but as *Homo faber*"(d) Your members must therefore realise that a casual perusal of stray journals cannot possibly supply either the incentive or the information necessary for progress in our work. A systematic examination of the abstracts and indexes of literature on his subject at least, should be a regular habit of the practitioner and the student The technique of collecting relevant information from ori-

(d) Si nous pouvions nous dépouiller de tout orgueil si pour définir notre espèce nous nous en tenions strictement à ce que l'histoire et la préhistoire nous présentent comme la caractéristique constante de l'Homme et de l'intelligence nous ne dirions peut-être pas *Homo sapiens* mais *Homo faber* H. Bergson :—*L'évolution créatrice*, Paris 22e ed. 1920 p. 181

ginal articles and discriminating that which is spurious and superficial from that which is sound and reliable needs training and intelligence "Understanding derives from an intelligent and discriminating study of past and present experiences, once attained it unbolts the doors to an understanding of further experiences Discrimination of true from false relies upon a practised faculty of criticism, and upon a firm grasp of the rules of evidence Understanding is the basis of progress and the vital flame in education, discrimination is the only sure defence against false doctrine and unsound practice" ¹ An old English writer has described four types of readers and you should strive to belong to the fourth type all throughout your active life "Sponges which attract all without distinguishing, Howre-glasses which receive and pour out as fast, Baggs which only retain the dregs of the spices and let the wine escape, and Sieves which retain the best onely "

I do not think I can do better than by terminating with a quotation from a great physician and a great lover of books His writings have influenced my intellectual development to such an extent that probably most of what is stated above, except its imperfections, may be taken as an imitation of his teachings "The organisation of a library means effort, it means union, it means progress It does good to men who start it, who help with money, with time and the gift of books It does good to the young men, with whom our hopes rest, and a library gradually and sensibly moulds the profession of a town to a better and a higher status A library after all is a great catalyser, accelerating the nutrition, and the rate of progress in a profession, and I am sure you will find yourselves the better for the sacrifice you have made in securing this home for your books, this workshop for your members" ²

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THE TREATMENT OF HABITUAL CONSTIPATION BY EXPLANATORY SUGGESTION

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Habitual constipation is apt to be regarded as one of those minor ailments with which sufferers are more or less at liberty to deal in their own pet way and I have known eminent physicians to feel just a little peeved when consulted for this complaint. Yet if we could calculate the amount of suffering it causes in the millions of its victims and the amount of money annually spent on its alleviation there can be little doubt that statistically it would rank high in the list of human afflictions. It does, therefore, from time to time, deserve a little serious thought.

Numerous authors, prominent among them Alvarez, have expressed the opinion that habitual or chronic constipation is a functional neurosis in the vast majority of cases. This undoubtedly correct interpretation of surely the most common of all human ailments deserves to be popularised with emphasis. The practical therapeutic implications of such a view cannot be too clearly and precisely stated, as is shown by the fact that the perverse practice of prescribing fancy diets, gymnastic antics, aperients, lubricants, laxatives, purges, and as ultimum refugium the daily enema is still almost universally resorted to. Even the instructed physician is placed before the alternative of elucidating the mysteries of a functional neurosis to a sceptical, intensely preoccupied patient who wants medicine not talk and on the other hand the simple expedient of suggesting some method of artificial evacuation, whereby his only concern need be that he finds out carefully what has already been tried and then sedulously prescribes a new trick which will within 24 hours give the patient tangible proof of his doctor's skill. Most practitioners follow the line of least resistance, yield to its temptations and adopt the second alternative. They boggle at the apparent difficulty of translating the mechanism of a functional neurosis into simple, comprehensible and convincing language and perhaps some are not familiar with the psychotherapeutic knack of soothing the patient's anxiety, putting his mind into a receptive mood and banishing his fears rather than augmenting them with new and unheard of terrors.

If habitual constipation is a neurosis, and there can be little doubt that this is so, it is certainly the most common functional disturbance in man, yet no patient would think of consulting a psychiatrist for constipation, nor would doctors dare to suggest such a thing to their constipated patients and yet strange as it may seem the psychiatrist would be the proper person to consult in the majority of cases. However, the treatment of habitual constipation will remain in the hands of the general practitioner and so a simple psychotherapeutic technique which he can always follow may be welcome.

Defining chronic or habitual constipation we may say that the term applies strictly to those cases in which there is no conclusive

evidence of organic disease such as piles, fissures, severe proctitis, polypus, constricting growths or scars, compressing tumours, loss of nervous control, the palpable presence of a large faecolith, Hirschsprung's disease, etc. An assumed chronic appendicitis, chronic "dysentery" with cysts but no occult blood in the stool, a "non-specific" colitis I do not regard as conclusive evidence, such cases are included in our present consideration as experience shows that many of them yield most satisfactorily to explanatory suggestion. I do not consider a person to be *suffering* from habitual constipation who normally has a motion once in three days or even once a week if he is healthy, well and perfectly satisfied with his slow rhythm and has the good sense to accept the position cheerfully, to resist all therapeutic blandishments and to treat such medical bogeys as intestinal toxæmia with the lusty contempt they deserve in a case such as his. Obviously we do not include cases in which there is a sudden and recent interruption of a previously normal rhythm as in the case of acute disease. Thus, then, our term applies to that large contingent of people whose suffering ranges from a mere intestinal "sluggishness" for which they take "a little daily dose" or "aid to digestion" to the person who is driven frantic by the fact that even the most violent purging will not bring about the desired result and relief. Somewhere between these two extremes lies that group of patients who have one or even several motions a day but are harassed by the conviction that these motions are entirely unsatisfactory.

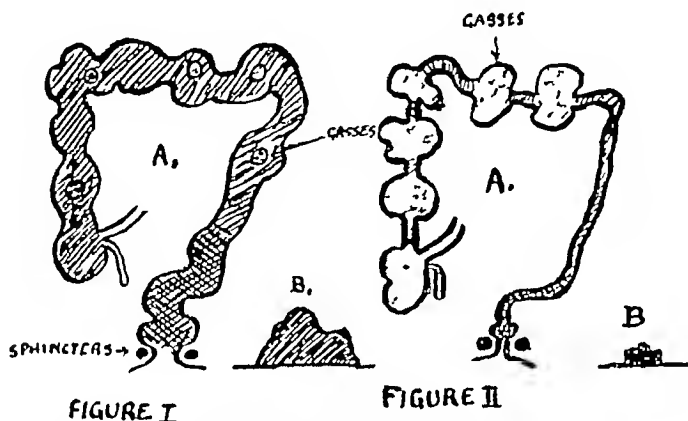
Strangely enough, and we may say fortunately, the abnormal condition which is responsible for all the variegated symptoms associated with or attributed to habitual constipation can be summed up in the few words—that it may be regarded as nothing more nor less than an abnormally *empty* colon. Such paradoxical generalization needs explaining. Two misapprehensions lie at the root of chronic constipation. The first is a totally unfounded notion that unless a copious stool is evacuated once or even twice a day there must be some serious obstruction. The patient is unaware of the scientific fact that the quantity of stool passed is not directly related to the quantity of food eaten but depends to a far greater extent upon the colonic bacterial flora and the water content of the faeces. It never spontaneously occurs to the patient that his small stool may be the simple result of the fact that his rectum and sigmoid do not contain more. He fears an obstruction and confirms his fear by the second misapprehension, namely, that his abdominal distension is caused by faecal stasis. He does not know that his heaviness and "gasses" are caused not by decomposing faecal masses, as he thinks, but are the inevitable result of colonic emptiness and spasms. Now as long as he labours under these erroneous notions he will necessarily choose the most irrational method conceivable to put matters right. He will do just those two things which he should scrupulously avoid, namely, purging and eating less food. If he understood the mechanisms involved he would refrain from attempting to have a stool for several days and eat *more* than his normal quantity of food which, if done with the happy confidence that this is the right thing to do,

would in a few days relieve his distressing colonic emptiness, his spasms, gasses, pains and indigestion. What is more he would enjoy the satisfaction of a regular, quick, smooth, easy and ample evacuation.

Now how can we convince our patients of this obvious and simple fact? A method which has given me most gratifying results is as follows. When you suspect a patient to be suffering from functional constipation try to put yourself into the frame of mind of a benevolent teacher called upon to help a child out of a hopeless muddle into which it has got itself through a silly misunderstanding. In this general attitude listen with attentive interest, to the patient's usually eloquent and dramatic account of his symptoms. Make a point of taking the words out of his mouth to which he reacts with an enthusiastic "Yes, that is just what I feel". Tell him, before he has a chance, that he has "gasses", that when he goes to stool he passes a tiny quantity and then starts straining because he has a feeling that there is lots more to come and that sometimes he has to sit for half an hour before he gets a further meagre evacuation. Tell him that his stool is often thin like a pencil or consists of hard little balls. Suggest that he has a loss of appetite because he "cannot digest his food", that he has noticed a loss of strength and energy and that even laxatives do not seem to help him. The result of such a conversation is that the patient is delighted to have at last found a doctor who takes him seriously and fully understands him, as he always thinks, *very special case*. Such an atmosphere of trust and cordiality is of course, an essential preliminary to all successful suggestive therapy and as soon as it is established you proceed to the next stage which is a grave and really careful physical examination. When you are satisfied that there does not appear to be any reason to suspect an organic lesion, roll the patient's descending colon with considerable pressure under the palpating hand. In all these cases the descending colon can be felt like a hard rope of less than an inch in diameter because it is spastic and empty. The patient can feel it too and you must call his attention to the fact. Then percuss the tympanitic areas which are always present in other parts of the colon and demonstrate the sound to the patient saying "You hear that, it is like a drum, those are the gasses you complain of". Then let the patient dress. Never talk to a patient while he is dressing. Let him sit down to listen carefully.

Confining yourself as far as possible to purely mechanical explanations and leaving out "psychology" altogether, say something like this. "Having examined you, your complaints are perfectly clear to me and I shall now try to explain to you exactly what is happening in your inside. This (draw a rough sketch as in fig I-A) is what a normal colon looks like. You see it is completely filled with faecal matter and any gasses that form in it can move about freely and without obstruction. Now when a person with such a normal colon has a motion he empties only the cross-shaded part and this produces a large normal quantity of stool as shown here (fig I-B). Such a person has a feeling that he has had a very

satisfactory motion During the next 24 hours the next portion moves down to fill the rectum Such a person has a good appetite and his intestines are perfectly comfortable, in fact, he is unaware of their functioning because they are always full as they should be Now I am going to draw a picture of *your* colon which looks like *this* (fig II-A) The dotted parts are distended with gasses These gasses cannot move on because the parts of your colon which lie between these distended parts are empty, contracted and cramped It is this hard, empty and contracted colon which you felt under my hand when I examined you If your colon had been full as in the first picture neither you nor I could have felt it Now you will see that when *you* have a motion and empty the shaded part of your colon it will only result in so much stool (fig II-B) which you naturally consider



Figs I and II explaining the mechanism of functional constipation

unsatisfactory and you, therefore, try to get out more This effort of yours, however, is bound to prove futile because there is actually no more stool to come Your straining and anxiety will only result in a cramp of your anal muscles which gives you a feeling that there is still something to be got rid of All you will produce by straining an empty rectum is piles Now the question arises how can we change your abnormal colon (fig II) into a normal one as shown in the first picture You will, I think, agree that this is very simple, all we have to do is to go on filling it from the top and close the opening at the bottom until your colon is full I can promise you that if you do this you will be permanently cured of all your troubles within a few days Disregard your loss of appetite and eat more than your normal quantity of food, any kind of food, force yourself to eat it Stop worrying about gasses, they will disappear by themselves as soon as your colon is full, and try your best not to have a motion for about 3 days On the 4th day you go to stool and try to have a motion but do not sit for more than half a minute, 30 seconds by your watch If in this time you have a motion well and good, if you do not, do not try longer, give up at once, wait till the following day and continue to take plenty of food If you do not have a motion on the 4th day it is not because

you are suffering from constipation, it is simply because you have not yet eaten enough to fill your colon. On the 5th day you will certainly have a large motion. Now I am not going to give you any medicine, you need none. Do exactly as I have told you and come back and tell me how you are getting on after 5 or 6 days."

Experience in hundreds of cases shows that if words to this effect are spoken to fairly educated patients (particularly the educated suffer from this complaint, not because they lead a sedentary life but because they are inclined to apprehensive introspection), with a maximum of supercharged energy, conviction and authority, the patient walks out of the consulting room in the half-dazed condition one might expect in a person who has seen a vision. All his cherished notions have been rudely shattered and he has suddenly seen a way leading straight out of a maze of fear, anxiety and utter hopelessness which threatened to make his life a misery. I should say that in about 85 per cent of the cases the method is so entirely satisfactory that the patient is overjoyed when he pays his second call and gladly admits that "it has worked." In spite of his scepticism. Of the remaining 15 per cent some return with further questions and doubts and some require the artificial help of atropine and a sedative to get the necessary relaxation.

It may be hardly necessary for me to point out that I do not pretend to have given a physiologically comprehensive or even correct interpretation of habitual constipation in a scientific sense. My object is merely to describe a psychotherapeutic manoeuvre which I have found to be successful. The time and energy spent on this method, which very soon becomes a technical routine, is well worth the results obtained.

Obviously it is not possible to adopt this elaborate method in the hustle of a large out-patient department where constipation is a common theme of exasperating monotony. On the other hand we, in our Hospital, being convinced that the majority of cases of constipation are functional, feel that prescribing and dispensing a purge when asked to do so by the patient is economically unsound and therapeutically irrational. We have, therefore, devised an abbreviated method which, during the 3 years it has been exclusively followed, has produced most satisfactory results. During this period not a single dose of any kind of aperient, lubricant, laxative or purge has been prescribed in the medical out-patient department for cases of functional constipation which represent a vast majority. When we diagnose a case as functional and having assured ourselves by palpation that the colon is empty, we simply assure the patient that his trouble is due to this fact. We advise him to increase the bulk of his usual food, to make it a rule to go to stool only once a day if possible and not to squat for more than half a minute. If in that time he does not have a motion he should never try a second time but wait until the following day. We also tell him that any kind of laxative will make him worse. We give no medicine and tell him to try this method first. It is surprising to see how many patients accept this simple advice and are thereby

relieved

Three further points should be borne in mind when practising this method. The first is that the normal evacuation of the bowel is a conditioned reflex. It is therefore desirable that the motion should always take place at a fixed point in the daily toiletary or dietary routine, it should always follow the same item of the daily morning schedule. Evacuation will then become largely automatic, require no conscious effort and the complicated interplay of nervous and muscular events will follow each other in a perfect sequence with perfect timing. The second important point is that fluid intake must be adequate, particularly in a hot climate. If the body runs short of water for perspiration and urine it will take what it can get from the intestinal contents which thereby become harder, drier and less voluminous. The third point is that some patients have a well-filled colon but suffer from a nervous spasm of their anal sphincters due to the anxiety and apprehension with which they go to stool. Naturally when these sphincters, almost as powerful as a clenched fist, are not relaxed no motion can pass with any amount of straining. If in these cases the patient observes the requirements of a conditioned reflex and can be taught to assume a happy indifference to whether he passes a stool or not for some days he will usually be relieved. It is particularly this type which sometimes needs antispasmodic and sedative medication for 3 or 4 days.

Finally, a few words about infantile constipation. It is a deplorable fact that it is not yet generally recognised that infants should never be given any artificial aid to evacuation. The abnormal consistency of an infant's stool is a matter of diet, not medicine. It is possible to give an infant's stool any desired consistency merely by altering the protein-carbohydrate ratio in the diet. Of course, there are exceptions, but the simple general rule is this. In purely breast-fed infants ignore loose and frequent stools as long as they contain neither blood nor mucous and the child otherwise appears healthy and thriving. When the infant is constipated and has hard, dry, infrequent and painful motions give sugar and water liberally between feeds until the stool has the desired consistency. In artificially fed infants add ordinary sugar to their feeds when they are constipated. When they have diarrhoea, first stop sugar, if this is not sufficient to check the diarrhoea give thin oatmeal or wheat cunjee and finally if necessary albumen water in addition to the normal feeds. While some of my readers may feel that I owe an apology for this apparent digression from my theme, I plead that the knowledge that it is so easy to regulate an infant's stool has a very salutary effect upon over-anxious parents who in my experience are only too apt to apply their own intestinal neurotic doctrines to their unwitting infants.

Summary

- 1 Chronic or habitual constipation, a functional nutrosis
- 2 Its treatment by explanatory suggestion
- 3 An abbreviated method
- 4 Infantile constipation

PAGET'S DISEASE OF BONE

A REVIEW WITH A CASE REPORT

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The horizon of the concept of Paget's disease has been progressively widening, since Paget's classic clinico-pathological description of the disease in 1876. His original report of five cases included cases recognised and reported previous to him by Wrony in 1867, and Wilks in 1869. He described the disease as a "form of chronic inflammation of bones"—osteitis deformans. Prior to him, Czerny in 1873 had designated the same disease complex as "osteitis deformans". In 1874 Benno Schmidt is reported to have described a similar bone lesion in a tibia.

Paget believed it to be a disease of modern times. However Dickson et al, of the Mayo Clinic, cite reports of paleo-pathological evidences of the disease occurring in pre-modern days. Denninger found morphologic and roentgenologic evidences in bones of American Indians excavated from the Illinois River Valley. Butlin, during his examination of Neanderthal skulls in the South Kensington Natural History museum, found changes resembling osteitis deformans (Dickson).

Hallermann, quoted by Groh, defines it as a specific mild disease with a persistent structural change, followed by bone absorption and degeneration, and secondary medullary fibrosis. The characteristic feature is a continued resorption and rebuilding of affected bones. Unlike osteitis fibrosa cystica generalisata, where porotic changes are more prominent, osteosclerosis and calcification are the distinctive features. The whole structure of bone, as stated by Butlin, seems to be almost entirely removed and replaced in a new design with increase in size of the affected bones. Bones at first are softened producing the tibial, femoral and other bendings characteristic of the disease. Later their resilience is lost and the bones become fragile. Although frequently polyostotic and progressive, it is not a generalised bone disease, as is for instance osteomalacia, etc. Different parts of the skeleton and even different parts of the same bone, manifest varying phases of the disease process. Such an occurrence is not possible if the disease were a generalised one.

Two definite forms of the disease are now recognised, the polyostotic and the monostotic form. Both these forms present microscopic pictures which are specific of Paget's disease. Jaffe thinks that histological appearances are of greater importance in the diagnosis of Paget's disease, than the clinical and gross morphologic appearances. Co-existing porotic and sclerotic changes are characteristic. To Schmorl goes the credit of bringing into prominence the specific microscopic picture of the disease. A typical Paget's bone consists of irregular segments of lamellar bone, separated by short irregular cement lines. The tiny fragments of lamellar bone are "fitted into one another like an irregular mosaic". Schmorl coined the term "Mosaic structure" for this appearance which is now considered typical of Paget's bone. As pointed out by Freund (Jaffe Lit.), there

is hardly any attempt by the lamellar bone to arrange itself round blood vessels to form haversian channels "The more rapid and the more florid the progress of the disease, the more characteristic is the appearance of this mosaic structure" As healing takes place the mosaic structure tends to disappear Associated with these changes in bony architecture are certain changes in bone marrow The myeloid and fatty marrow is converted into fibre marrow There is a large number of engorged vascular channels in this altered marrow with large quantities of blood pigment There is a great tendency to spontaneous healing with disappearance of the mosaic structure The more gradual the progress of the disease, the less typical is the mosaic structure

Certain atypical forms of the disease are also reported In some of these the bones especially the vertebra and the sacrum show dense sclerosis, in which a very atypical mosaic structure is seen microscopically This is attributed to the relatively gradual progress of the disease

In typical Paget's when the disease affects the long bones, Brailsford believes the spread occurring via the periosteum or the endosteum or sometimes both When the spread occurs via the periosteum, the latter is gradually elevated from the surface of the bone, by growth of osteoid tissue Jaffe cites, Pick and later Stenholm and Christeller to have described an endosteal form of the disease The disease was localised in the marrow cavity with little change in the tubular bone Jaffe states that if these are really cases of Paget's disease, then the atypical appearances should be attributed to a healing tendency

Patient with advanced polyosteotic form of the disease presents a typical simian appearance, there is the stooping with rounded shoulders, the enlarged head with frontal bosses, carried forwards, the approximation of the lower costal margins to the pelvic brim, the abdominal bulge, the loss of height, with the lower limbs held apart, the femora bent sideways the tibial bones thickened with anterior bowing, the upper extremities, apparently longer than normal, hanging by the sides Although the fully developed disease appears symmetrical the progress of the disease is asymmetrical affecting first one bone or part of a bone, for instance a sacrum or a tibia, than affecting a distant bone such as the skull or a vertebra Prevailing idea about the rarity of this disease is not true It is often asymptomatic and therefore is not noticed clinically Advent of Roentgen rays has shown it to occur more often than was believed upto now Often the presence of the disease is recognised accidentally during routine roentgen examination of the urinary tract 27 of Gutman and Kasabach's 116 patients, and 75 patients in a series of 367 cases of Paget's collected by Dickson et al of the Mayo Clinic, were asymptomatic

When present, the commonest symptoms are, backache, headache, pain in the legs and hips and fatigue But the disease may be present for a number of years without producing any symptom

The tibia was, at first, believed to be the bone most commonly affected In a series of 154 cases examined by Brailford, the disease

was found to have affected the pelvis in 58 cases and the tibia in 37 cases. In the 367 cases examined by Dickson, pelvis was found to be the most frequent site. Schmorl's systematic studies of a few thousand skeletons, showed the spine and the sacral bones to be the commonest sites involved. Schmorl suggested and confirmed by his studies that the site of involvement to a particular bone is related to the frequency of the mechanical effects of function and trauma to which the bones are subjected. Sacrum is the part of the skeleton carrying the weight of the torso and hence probably the frequency with which it is involved. This view also gains support from the fact of the frequent occurrence of the disease in the pelvis and lower extremities, Jaffe states that the frequent involvement of the skull and jaw bones, however, cannot be explained. Less frequent sites are the femur and the humerus, small bones of the feet are sometimes the sites of involvement among these the os calcis is the commonest.

Age Incidence

The disease, usually, is found after the middle age, less commonly it is found in earlier age periods. Among Brailford's 154 cases 106 were between 50 to 70 years age period, 24 between 40 and 50 years. Youngest age at which definite evidence of the disease was found was 27 years. Dickson's 367 cases showed the following age incidence when the diagnosis was made: 29 cases between 30 and 39 years, 70 cases between 40 and 49 years. Between the age period 50 and 70 years there were 231 cases. Kay and her associates (quoted by Dickson) found in their 34 cases, the average age to be 55 years.

Biochemical Findings

A reference to certain biochemical changes would not be out of place. Normal concentration of calcium per 100 cc of serum is 9 to 10.5 mg, concentration of phosphorus is 3.3 per 100 cc of plasma. In the cases of Paget's analysed by Kay the average concentrations of calcium and phosphorus were 9.1 mg and 3.7 mg respectively. Dickson's cases show the averages of 9.8 calcium and 3.48 for phosphorus. Kay and her associates in 1929 for the first time showed an elevation of plasma phosphatase in osteitis deformans. The enzyme is also increased in osteitis fibrosa, osteomalacia, etc., Roberts in 1930 confirmed the above results of Kay.

Another important chemical change is the increase in alkaline phosphatase in the serum. Dickson reports on the change in alkaline phosphatase activity in 101 cases of Paget's. The variation ranged from 1.3 to 216 units. There is found to be general relation between amount of alkaline phosphatase and the extent of the bone involvement. Greater the bone involvement, the larger the amount of alkaline phosphatase. There is marked disturbance of mineral metabolism. There is retention of calcium, magnesium, phosphorus. Calcium excretion through urine is diminished. Further Gutman, Gutman and Robinson in their investigation on the "acid" phosphatase activity of serum in skeletal metastasis from prostatic cancer and Paget's disease found that in most cases of the former the acid phosphatase activity in serum was greater than 3.0 units per 100 cc.

(normal 0.5 to 2.5 units) In Paget's disease on the other hand only in the very advanced cases with high alkaline phosphatase activity were the acid values higher. Roentgen and clinical changes were sufficient in these for diagnosis. On the other hand early cases of Paget's disease with sclerotic bone changes showed normal values of the acid phosphatase activity. They express the opinion that determination of "acid" phosphatase activity in serum in early cases of Paget's disease may be helpful in differentiating the sclerotic skeletal changes from those produced by Secondaries from prostatic malignancy.

Roentgen Manifestations

With the development of Roentgenographic technique, diagnosis of Paget's disease, as with many other clinical conditions, has become fundamentally a roentgenologic problem. Particularly this is so with the clinically atypical and less advanced types of the disease. The present day recognition of the monosteitic form as a separate disease entity is mainly due to roentgen investigations.

The earliest change that could be noted is the condition of acute osteitis which occurs in the beginning of the development of the disease. This is however not noted so often, as the patients are examined mostly in the later phases of the disease. Three chief varieties of roentgen appearances are seen. These are the osteoporotic, the sclerotic and the combined type of lesions. These changes may be seen singly or in combination, in the same bone, or in different bones at the same time.

Vertebrae

In the osteoporotic type, there is marked osteoporosis, with widely separated, coarsened, dense trabeculae. These changes are seen in the central part of the bones, surrounded by a relatively sclerosed shell which is made of dense cortical trabeculae herded together. There is a tendency for the vertebrae to collapse, with an increase in size of the transverse and/or anteroposterior diameters. The affected vertebra thus appears larger than normal. Similar appearances of increased trabeculations and increase in size are produced by haemangioma of the vertebra.

The second type affecting the vertebra produces, a densely sclerosed vertebra, with increase in its transverse and/or anteroposterior diameters, but there is no tendency to collapse. This type has to be differentiated from sclerotic type of metastasis, or a beginning Albers-Schönberg's disease. In advanced polyostotic lesion many of the vertebrae may be affected with collapse and surrounding sclerosis leading to the decreased height of the person. Even the osteophytes associated with spondylitis may show these changes. As reported by Schmorl, Groh, etc. the disease may remain localised to a single vertebra without involvement of any other bones of the skeleton.

Pelvis

Part or whole of the pelvis may show roentgen evidences of the disease in one or more of its phases of development. Brailsford describes, an osteoporotic, osteolytic or sclerotic, and the lithocystic or combined type. The osteoporotic pelvis shows marked decalcification

with increased trabeculation and deformity This form occurring singly is extremely difficult to differentiate from osteomalacia or Von Rocklinghausen's disease

The sclerotic type presents densely sclerosed pelvis or part of it and has to be differentiated from Albersn Schonberg's disease, and metastatic sclerosis from prostatic or gastric malignancy The combined type of lesion is more common, here part of the pelvis usually the upper part of the iliac bones show the lytic changes, the parts surrounding the acetabula and the brim show dense sclerosis whereas the ischia and the pelvis may show cystic appearances, or the whole pelvis may be studded with rounded nodosities with woolly margins scattered in a decalcified matrix Differentiation from secondary carcinomatous metastasis is difficult Sutherland of the Mayo Clinic, is however of opinion that the scattered sclerosis in the two conditions could be differentiated by the maintenance or acceleration of the trabecular elements in osteitis as against obliteration of the trabeculae in metastasis Besides in osteitis the laying down of subperiosteal bone produces an increased size of the bone, which is not found in metastasis

Skull

Like other parts of the skeleton the calvarium presents varying appearances Earliest change seen is the presence of ill-defined areas of osteolysis in the frontal or temporal bones, or there may be osteolytic stippling associated with larger areas of osteoporosis, or there may be a large area of osteoporosis circumscripta, the term first coined by Schuller This appearance occurs aside of Paget's disease but is often found as an early manifestation of Paget's Gutman also was one of the first to describe this appearance in Paget's Pines, quoted by Jaffe, also described a porotic type of skull without associated sclerosis

Later there appears woolly nodular opacities scattered between the inner and outer tables of the calvarium Usually such a change starts on the inner table whose outer border cannot be differentiated The outer table at first remains well-defined The sclerosis is associated with increase in size of the skull, but this increase does not take place at the expense of the cranial cavity At first the vascular markings and the sutures remain well demarcated but with the progress of the disease—the vascular and sutural details are lost During the porotic phase the basal angle of the skull is increased with production of varying degrees of platybasia

Tibia

Tibia is one of the long bones which presents some of the most characteristic roentgen appearances In early stages a generalised hellsterasis with ill-defined trabeculation and faint ground glass appearance is present as in the case published by Dickson During the porotic stage there is a bowing of the bone, later the progressing porosis produces—widened, coarse, dense trabeculation This trabeculation presents a vertical parallelism Sclerosis is first evidenced mostly on the anterior surface—which is produced by subperiosteal, laying down of bone This appearance has to be differentiated from

the saber tibia seen in syphilis. The distinguishing appearance is said to be the involvement of the epiphyseal ends of the bones which in Paget's shows widened, sclerotic trabeculae arranged in a vertical parallel fashion. There is no such involvement of the ends of bones in syphilis, sometimes the sclerosis is seen on the concave surface of the tibia. The involved segment of the bone shows abrupt separation from the normal bone. As mentioned previously Brailsford expresses the opinion that the disease may develop via the periosteum or/and less often the endosteum. Both the cortex and medulla are later involved and show the characteristic appearances. Femora show similar changes with a bending in the lateral direction. The os calcis is frequently the seat of involvement—presenting the typical widely separated dense trabeculation.

Complications

The three complications of the disease are now well-known. These are, fractures, sarcomatous degeneration and the so-called pseudo-fractures or looser's zones. The commonest is the occurrence of fractures, these occur with slight injury and are as a rule transverse and "chalk" like. Healing usually takes place normally and the callus also sometimes show typical Paget's bone changes.

Malignant Degeneration

Five of Paget's first cases died of malignant degeneration. Brailsford reports sarcomatous changes only in six of his 154 cases. He expresses the opinion that a further follow up of his cases would give a much higher incidence of sarcomatous changes. In 8 per cent of the 66 cases reported by Pack et al in 1901, sarcoma was found to complicate Paget's disease. Dickson cited the following percentages of incidence of sarcomatous complication reported by various workers. DaCosta in 1915 found 9.5 per cent of his cases undergoing malignant change. Speiser in 1927 reported 6 sarcomas in 150 cases. Bird's review of 64 cases of Paget's showed sarcoma in 7 cases. An analysis by Coley and Sharp of the cases referred to the American Registry of Bone Sarcoma, showed that between the age periods of 50 to 70—40 per cent of osteogenic sarcomas were found in association with Paget's disease. Dickson et al found 3 cases of osteogenic sarcoma and 1 of benign giant cell tumour in their cases of Paget's disease. Frequent association of sarcomatous degeneration with Paget's disease is now confirmed. Certain peculiarities of malignant degeneration in Paget's are noteworthy. There is often an occurrence of multiple malignant foci. Brailsford thinks that malignant change may start as subperiosteal, endosteal or subdural tumours. Multiple such bony deposits may be found without involvement of the viscera, this is contrary to what happens in unassociated sarcoma, where pulmonary metastasis is an usual event. Davis and Cooke express the opinion that occurrence of malignant change in multiple distinct foci is undoubted. Post-mortem examination by them showed no pulmonary and visceral metastasis to suggest blood borne dissemination from a single focus.

Looser's Zones

Roentgenograms of affected bones sometimes show transverse radioluscent zones extending from the convex border to the nearby

medullary edge. These transverse zones have slightly sclerosed borders. Nature of these so-called pseudo-fractures is not definitely known. But they are believed to be produced by absorption of cal-



Figs 1 and 2 Showing typical appearance of the patient. Note the swelling on left leg. Fig 3 X ray of the ends of the left femur and tibia showing prominent trabeculation and cancellation and sarcomatous destruction of the upper part of tibia. Fig 4 X ray showing marked trabeculation with osteolysis in the calcaneus talus and other tarsal bones. Fig 5 X ray of the pelvis showing sclerosis of the pelvic bones with scattered cystic areas. Fig 6 Lateral X ray of the skull showing Sclerosis of the inner table in the anterior half and scattered nodules between the outer and inner tables.

cium along lines of stress. Dickson considers them to be incomplete fissure fractures and cites Schmorl's microscopic study in which the latter regarded them to be true fissures produced by trauma.

Etiology

Nothing is definitely known about the causation of Paget's. Probably one of the reasons is the tendency to assign a single cause for the production of this symptom complex. Various factors have been held responsible for the disease. These include, trauma, chronic infection, absorption of toxius, endocrine disturbance. Paget considered it to be a form of chronic inflammation of bone. Syphilis was thought to be the cause of Paget's particularly by certain French investigators. Out of Dickson's 367 cases, only 11 gave positive Wassermann. Incidence of positive Wassermann reactions in the cases reported by Key, Gutman, etc. is also very low.

Certain investigators believe the disease to be a slow infectious process and cite as evidence the clinical picture of infection found in many cases of Paget's.

CASE REPORT

A Gujarati male (Figs 1 and 2) aged 70 years, was referred to the Tata Memorial Hospital on 2-8-1945 for swelling and pain in the upper part of left leg. He had progressive deformities of the limbs for the last 15 years. Difficulty in walking—5 years, pain in the limbs, 2 years. He had enlarged head with frontal bossing. Rounded shoulders with deformity in both arms. Dorsal kyphosis with approximation of costal margin to the pelvic brim. Both femora and tibia were thickened and bent. Clinical diagnosis of Paget's disease was given.

RELEVANT LABORATORY FINDINGS

Serum calcium	14.4 mg %
Phosphorus	3.6 mg %
Alkaline phosphatase	8.4 units (normal 1.5 to 4 units)
Acid phosphatase	1.9 units (normal 0.5 to 2.5 units)
Red blood cells	3.0 millions
White blood cells	5.1 thousands

Radiograms of the skull (Fig 6), Pelvis (Fig 5), Tibia with sarcomatous changes (Fig 3), Calcaneus (Fig 4) show the typical appearances in the various phases of the disease as described in the text. Figure 3 shows the involvement of the ends of long bones with coarse widened trabeculation.

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(continued from page 124)

Pethidine Hydrochloride
Pheniodol
Pholedrine
Propamidine
Soluble Phenytoin

Dolantin, Demerol
Billselectan
Veritol

Phenytoin Sodium, Soluble
Dilantin, Epanutin, Solanolin

Stilbamidine
Sulphadimethylpyrimidine
Thiomersalate

Sulphamezathine
Merthiolate

Critical Notes & Abstracts

OFFICIAL AND APPROVED NAMES OF SOME NEW DRUGS

<i>Official Names</i>	<i>Other Names</i>
Acetarsol	Stovarsol
Amethocaine Hydrochloride	Decicaine' Tetracaine
Amphetamine	Benzedrine
Amphetamine Sulphate	Benzedrine Sulphate
Bromethol	Avertin
Carbachol	Doryl, Moryl
Chinlofon	Yatren
Chlorocresol	Parachlorometacresol
Chloroxylenol	Parachlorometamyletol
Dithranol	Cignolin
Hexobarbitone	Evipan
Iodoxy	Uroselectan-B
Leptazol	Cardiazol, Cartazol
Menaphthone	Menadione
Mepacrine Hydrochloride	Atebrin, Quinacrine, Meta- quinine
Mepacrine Methanesulphonate	Atebrin musonate
Mersaly	Salyrgan, Esidrone, Novurit Neptal,
Nicotinamide	Niacinamide
Nikethamide	Coramine
Pamaquin	Plasmoquin
Pemitone	Prominal
Silver Protein	Protargol
Sodium Bismuthyltartrate	Sobita
Soluble Hexobarbitone'	Evipan Sodium
Soluble Pentobarbitone	Nembutal
Soluble Thiopentone	Pentothal Sodium
Stibophen	Fouadin
Stilboestrol	Diethylstilbestrol
Sulphacetamide	Albucid
Sulphanilamide	Prontosil Album
Sulphapyridine	Dagenan, M & B 693
Sulphathiazole	Thiazamide, Cibazol
Suramin	Germanin, Bayer 205, An- trypol
Theophylline with Ethylenediamine	Euphyllin, Aminophyllin
<i>Approved Names</i>	<i>Other Names</i>
Cyclobarbitone	Phanodorm
Desoxycortone Acetate	Deoxycorticosterone Acetate
Dicoumarol	Temparin
Dienoestrol	
Dimethylstilbamidine	
Diodone	Perabrodil
Diphenan	Butolan
Ethisterone	Ethinyltestosterone
Hexazole	Azoman, Triazole
Meprochol	Esmodil 0.3 per cent iso- tonic solution
Mesulphen	.. Mitigal
Pentamidine	

(continued on page 123)

DIAGNOSIS OF BONE TUMOURS BY ASPIRATION

A REVIEW OF 80 CASES

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Tumours of bones or of adjacent tissues in their early stages present many difficulties for a reasonably correct diagnosis. In its absence the attending physician loses valuable time in ineffective and sometimes harmful measures. An early recognition of these tumours is of vital importance to the patient in most cases. Three procedures are available for arriving at a correct diagnosis, viz clinical examination, radiographic study and a histological investigation of morbid tissue. All of them are subject to certain limitations and possess respective advantages. The best results are obtained by co-operation between the clinician, the radiologist and the pathologist, rather than by rivalry between the three disciplines. There is hardly any justification for statements¹ regarding the unreliability of one or other method, as individually they are all of them insufficient and only collectively afford the largest measure of assistance. Codman² has pointed out that in properly equipped institutions the majority of cases of osteogenic sarcoma are usually promptly diagnosed, independently in each of these three departments, but that if "either the clinician, roentgenologist or pathologist has any doubt then probably all should have and do have doubt."

The clinical examination and radiographic study in expert hands is unattended by any pain or risk to the patient. The removal of tissue from the suspected tumour is, however, dangerous in unskilled hands, and is not entirely immune from all risks even with experts. These dangers have been previously discussed⁵ and need not be mentioned again, except to state that the risks of the procedure become negligible if proper care is exercised in biopsy technique. The untoward consequences of an incisional biopsy are a rupture of the tumour capsule, haemorrhage in the tumour substance and a dissemination of tumour cells. These are often followed by infection or fungation of tumour tissue through the biopsy wound. Coley³ has stated that "these bad results can largely be eliminated by greater care and more thorough understanding of the proper technique, and that its advantages outweigh its disadvantages."

The necessity for a biopsy becomes evident to any person who sees a certain number of bone tumours in the course of his routine work. The clinical and roentgenological diagnosis is often inadequate for planning a course of treatment. It is also difficult to eradicate all doubt regarding the effects of treatment on a particular type of bone tumour unless the microscopic structure has been previously established. It is believed that the existing serious outlook for patients with malignant tumours of bone could only be lightened by a more accurate understanding of the biology of such tumours. One is, therefore, obliged to steer clear of the Scylla of unnecessary cutting into the substance of a bone tumour and the Charybdis of renouncing the indispensable method of biopsy diagnosis.

During the last two years we have been attempting to elaborate a technique of aspiration biopsy which eliminates most of the disadvantages of incisional biopsy and yet supplies sufficient tumour tissue in most cases for a histological diagnosis. No originality is entailed in the technique described below and it would certainly be foolish to claim infallibility for any laboratory procedure. A trocar or a needle for obtaining a small piece of tissue has been occasionally used for almost fifty years. The staff of the Memorial Hospital in New York have perfected a technique which has proved highly satisfactory in their hands. They have very recently reaffirmed their view that aspiration biopsy is a valuable and reliable diagnostic procedure in bone tumours, and that "there have been no immediate complications of the procedure and no evidence to suggest more rapid development of metastasis by the use of aspiration to establish diagnosis"⁹ Unfortunately, smears of aspirated tissue destroy the neoplastic arrangement of cells and make it extremely difficult, if not impossible, to interpret their exact nature. Martin and Stewart⁷ feel confident that such interpretation "is not difficult provided the pathologist will learn by smearing out gross specimens received in the laboratory and comparing the pictures produced with the actual structures of the eventual section." We have found it easier and more reliable carefully to fix, embed and cut the tissue obtained by aspiration, and feel no hesitation in recommending it as a routine procedure in the case of all tumours in or near bones.

Technique

- 1 The first essential for any tumour problem in relation to bones is a meticulous recording of clinical information carefully and systematically obtained. Ewing has rightly stressed the importance of a history of persistent unexplained pain in an otherwise healthy person. The clinical examination is followed by a study of properly exposed radiographs designed to disclose (a) an alteration in the texture of the original bone, (b) the laying down of new bone, and (c) the limits of tumour extension in adjoining soft tissues. Particular attention is paid to any breach in the cortical bone or a thinning of the cambial layer, and every effort is made to determine the exact location of such a spot. The selection of a proper site for insertion of the aspirating needle and its direction is decided upon with the radiographic picture in full view.

2 The technique of aspiration has been admirably described by Martin and Ellis⁶, and as the original article may not be easily available in this country, the following section is reproduced from their paper "The skin at the site of the intended puncture is painted with iodine and a small area of skin infiltrated with 1 per cent novocaine. With a bistoury pointed scalpel (No 11 Bard Parker blade) a stab wound be made through the skin with the instrument held at right angles to the skin surface. This puncture of the skin facilitates insertion of the needle. An 18-gauge needle 5-10 centimeters in length attached to a tightly fitting 20 c.c. Record syringe is then inserted and advanced slowly through the superficial tissues until the point is felt to enter the suspected neoplastic mass. Guided by palpation with the disengaged hand, it is striking how readily a difference in consistence of the tissues can be felt as the needle enters a mass of neoplasm. When the point of the needle is felt to enter the tumour the piston of the syringe is partly withdrawn so as to produce a vacuum and the needle slowly advanced one to three centimetres farther, depending on the anatomy and size of the tumour. Maintaining the vacuum, the needle is then withdrawn to the same distance and advanced again. This manipulation may be repeated two or three times at the discretion of the operator, *care being taken to maintain the vacuum when the needle is advanced or partly withdrawn*. Aspiration with the needle at rest is not sufficient to draw tissue into the needle in most cases. By advancing the needle and aspirating simultaneously, a plug of tissue is both forced and drawn into the needle. Maintaining suction during partial withdrawal detaches the plug of tissue already within the needle. We have found this detail to be very essential. Before the needle is completely withdrawn from the tissue, the piston must be slowly released until the pressure in the needle is equalized, or better still the syringe detached and the needle withdrawn separately, otherwise the aspirated material will be suddenly drawn and splashed over the interior of syringe, making its collection difficult. While the needle is being advanced and withdrawn under negative pressure, a small quantity of blood mixed with fragments of tissue may enter the syringe, or a solid cylindrical mass of tissue may appear. In other cases, especially in the firmer masses, the syringe apparently remains empty, but after withdrawal, the needle is usually found to contain a plug of tissue."

3 The aspirated material in the syringe and in the needle is collected on a piece of white muslin cloth spread in a petri-dish containing normal saline. Before clearing the syringe, the needle should be detached and a few ccs of saline aspirated in the barrel. The material is then emptied on the muslin after removing the piston. The tissue in the needle could be gently pushed with a trocar.

4. The different steps in the technique have been described in the appendix, to facilitate reference. The features worthy of note are the use of a celloidin sac for processing bits of tissue, and the decalcification of fragments after paraffin embedding.

Salient elements of the Technique

1 The essential conditions for a successful aspiration are that

the needle should be sharp, the syringe well fitting and the operator conversant with the feel of bone tumours. The needle should be introduced slowly, deliberately and with a definite aim in view.

2 The clotted blood retaining the tumour tissue is detrimental to satisfactory histological sections. The tissue in the needle and the syringe is rocked about in saline to wash away the red blood cells. If blood clots are found in the syringe they are dropped in the fixative, and gently detached from tumour fragments, after a short time. This is facilitated by the dark brown colour of the blood and a pale yellow colour of tumour tissue after half an hour in Zenker-Formol.

3 It is essential to use clean unused paraffin for embedding, as fragments of tissue from previous biopsies may lead to deplorable errors.

4 The fixation in Zenker and the use of decalcifying fluid necessitates a longer time for nuclear stains.

Interpretation of slides

Familiarity with tumour histology, patient examination of all the aspirated material and repeated review of former experience is necessary before embarking upon a diagnosis of aspiration material. There have been occasions when a minute clump of tumour cells, with appropriate arrangement has been enough for arriving at a correct interpretation. There are certain tumours of the bone which elude all attempts at diagnosis with all the available means at our disposal. It is probable that with a better understanding of the biological alterations during neoplasia, we may hope to improve our skill at diagnosis. It would, therefore be, presumptuous to expect at present a correct diagnosis in almost every case of aspiration biopsy.

Evaluation of Results

Thirty patients with suspected bone tumours were studied during the last two years with a view to assessing the utility of this technique. These cases represent most of the commonly occurring tumours and there is no reason to believe that the successes or failures would differ materially in other hands. The table on page 129 summarises the data pertaining to the points raised above.

It is seen from the table that in 25 out of 30 patients it was possible to obtain some tissue from the tumour in the aspiration needle. In all except one of these 25 cases it was possible to arrive at a definite histological diagnosis on the basis of the aspirated material alone. The diagnosis was different from the X-ray diagnosis in 14 cases and was shown to be correct by further evidence derived from an incisional biopsy, operative specimen or response to treatment. In no case was a false diagnosis given in this small series. In six cases the three methods independently arrived at the same diagnosis. Only blood was aspirated in five patients and no material was available for histological examination. This failure may be due to insufficient experience with the technique, the structure of the particular tumour which was being aspirated or the deficiencies inherent in the method. We believe that all these three factors were responsible in our cases and we hope that with a larger experience we would be in a more favourable position to assess the

TABLE

Serial No	Case No	Age Yrs	Sex	Part Aspirated	Clinical Diagnosis.	X ray Diagnosis.	Aspiration Biopsy	Diagnosis.
*1	5282	53	F	Rt. Scapula acromion	Giant Cell Tumour Scapula	Osteolytic Osteogenic Sarcoma	Plasma Cell Myeloma	
2	5412	9/12	M	Occipital bone	Neuroblastoma with multiple metastasis	Skull with extensive bone defects and destructive changes in Femur Tibia, etc	Malignant Tumour	
*3	5016	13	M	Rt. Humerus upper end	Osteogenic Sarcoma	Osteogenic Sarcoma predominantly Osteolytic	Ewing's Tumour	
4	5768	40	M	Femur lower end	Osteogenic Sarcoma	Osteogenic Sarcoma	Chondro-Sarcoma	
5	5018	53	M	Rt. Femur upper end	Myeloma (multiple)	Giant Cell Tumour	Chondroma.	
6	6373	37	M	Rt. Tibia upper end	Benign Giant Cell Tumour	Benign Giant Cell Tumour or localised Fibro-Cystic Disease	Osteitis Fibrosa Cystica	
7	6520	11	M	Lt. Femur lower end	Osteogenic Sarcoma or Ewing's Tumour	Osteogenic Sarcoma	Osteogenic Sarcoma	
8	6567	12	M	Rt. Clivicle outer end	Sarcoma.	Osteogenic Sarcoma	Osteogenic Sarcoma.	
9	7361	24	M	Lt. Pubic bone	Ewing's Tumour	Ewing's Tumour	Ewing's Tumour	
10	7759	20	M	Rt. Fibula upper end	? Sarcoma Fibula	Osteogenic Sarcoma	Osteogenic Sarcoma.	
11	8166	20	M	Rt. 8th Rib	Chondro-Sarcoma or Ewing's Tumour	? Chondro-Sarcoma	Chondro-Sarcoma.	
12	8304	58	F	Rt. 7th Rib	Not stated	Bone Cyst? or Giant Cell Tumour?	Only blood clot	
13	8356	4	F	Skull Lt. Frontal	Ewing's Tumour	Osteogenic or Ewing's tumour	Ewing's Tumour	
14	8665	15	M	Lt. Ilium	(1) Sarcoma Pelvis (2) Retroperitoneal Dermoid (3) Ewing's Tumour	Osteogenic or Ewing's tumour	Ewing's Tumour	
15	9017	0	F	Lt. Femur	Sarcoma? Osteomyelitis	Ewing's Tumour	Ewing's Tumour	
16	10037	28	M	Rt. Ilium	Benign Giant Cell Tumour	Benign Giant Cell Tumour	Benign Giant Cell Tumour	
17	10155	58	M	Lt. 3rd Rib	Sarcoma in middle third of Rib	Soft tissue shadow Partial erosion by neoplasm	Metastatic Carcinoma.	
18	10315	58	M	Lt. Ilium	Osteogenic Sarcoma	Primary Tumour of bone sarcoma	Primary Lipogenic Sarcoma, of bone	
19	10409	30	F	Rt. Femur lower end	Globular swelling of lower thigh 30' diameter Osteogenic sarcoma Ewing's Tumour or Chr Osteomyelitis	Osteogenic Sarcoma	No tumour tissue in aspirated material	
20	10519	10	F	Rt. Fibula lower end	Ewing's Tumour or Chr Osteomyelitis	Ewing's Tumour	No tissue in aspirated material	
21	12095	70	M	Rt. Femur lower 1/3rd	Ewing's Tumour with pathological fracture	Ewing's Tumour	No tissue in aspirated material	
22	12225	37	M	Lt. Scapula	Tumour Lt. Scapula with metastasis in Lt. Supraclavicular & Axillary region	Osteogenic Sarcoma or Chondro-Sarcoma	Unusual type of Sarcoma probably Lipogenic.	
23	12288	52	M	Lt. Femur	Osteogenic Sarcoma	Osteochondroma	Osteogenic Sarcoma.	
*24	12502	11	F	Lt. Tibia upper end	Osteogenic Sarcoma or Fibrosarcoma	Chr Osteomyelitis with small sequestrum	Ewing's Tumour	
*25	12463	65	M	Humerus upper end	Osteogenic Sarcoma	Primary bone Tumour	No tissue could be obtained	
*26	12212	45	M	Lt. Buttock	Osteogenic Sarcoma or Fibrosarcoma	Chondro-Sarcoma	Chr inflammatory tissue	
27	13117	69	M	Bone aspirated left 7th rib	Myeloma	Myeloma	Metastatic deposit of squamous carcinoma	
28	13134	23	M	Right Ilium	Metastatic Carcinoma	Primary bone Tumour of right Ilium	Ewing's Tumour	
29	13101	20	M	Right Humerus	Osteogenic Sarcoma	Ewing's Tumour	Ewing's Tumour	
30	13250	24	M	Right Ilium	Osteochondroma	Chondrosarcoma	Ewing's Tumour	

Note—Numbers marked with an asterisk have been discussed in the text later

exact value of this technique. A study of this small series, however, indicates that the technique is deserving of a more extensive trial by surgeons and pathologists.

Representative Cases

Case 1 § 5282 A 53 year old married woman was admitted to the hospital with a complaint of pain and swelling over the right shoulder for the six previous months. She stated that she had similar pain in the same region about 4 years earlier which had lasted for 2 to 3 months and had later subsided without treatment. She had noticed a painful swelling over the shoulder 2 months before admission to the hospital. The skin over the swelling had become red during five weeks. On examination a rounded swelling situated over the point of the right shoulder was seen (Fig 1). The swelling extended towards the chest upto the outer quarter of the clavicle, down the arm for about 5 cms. and posteriorly up to the middle of the spine of the scapula. The swelling was "bright red as a tomato" and showed dilated capillaries on the surface. The tumour had been aspirated by a doctor outside who had found only blood in the syringe. The tumour appeared to be attached to the outer end of the scapula. It showed fluctuation and faint pulsation. Movements at the shoulder joint were normal except for abduction which was limited. Deltoid muscle and the anterior fibres of the trapezius were wasted. *Provisional Diagnosis* Giant cell tumour of scapula. The X-ray examination showed marked destructive changes in the upper border of the scapula and the acromion process. The latter had undergone considerable destruction and was represented by a thin flake of bone. Skiagram of the skull and other bones of the body were negative. *X-ray Diagnosis* Osteogenic Sarcoma (Fig 2). Blood examination showed the following—Blood sugar—95.2 mgms %, Serum N.P.N—160 mgms %, Phosphorus—44 mgms %, Phosphatase—36 B Units, Calcium—104 mgms %, Albumin Globulin ratio—1.1, Bence Jones Protein was absent in the urine. Kahn test was negative. The tumour was aspirated and examined as described above. It was reported as Plasma Cell Myeloma (Fig 3). The patient was treated by radiation, 3500 r in 45 days. The pain disappeared completely during the period of treatment. The patient was admitted a month later with severe pain in the lower part of the back and two small lumps over the vertex of the skull. They were treated with radiation and regressed. Three months later the patient complained of pain in the left temple, double vision and left abducent nerve paralysis. A month later she noticed pain in the left ribs and front of the chest. She improved with radiation. A month later she was readmitted with fracture of the upper part of left humerus and pain in the upper part of the left femur. Bence-Jones proteins were present in the urine at that time. The patient expired at her home nine months after first examination at the hospital with multiple lesions of myeloma of bones.

Case 2 § 5616 A 13 years old Hindu school boy was admitted with history of pain and swelling in the upper part of the right arm. The boy had a fall about 4 months previously and began to get pain in that region, although there was no swelling. One month later

Fig 1 Photograph showing a rounded swelling situated over the point of the right shoulder (§ 5283)

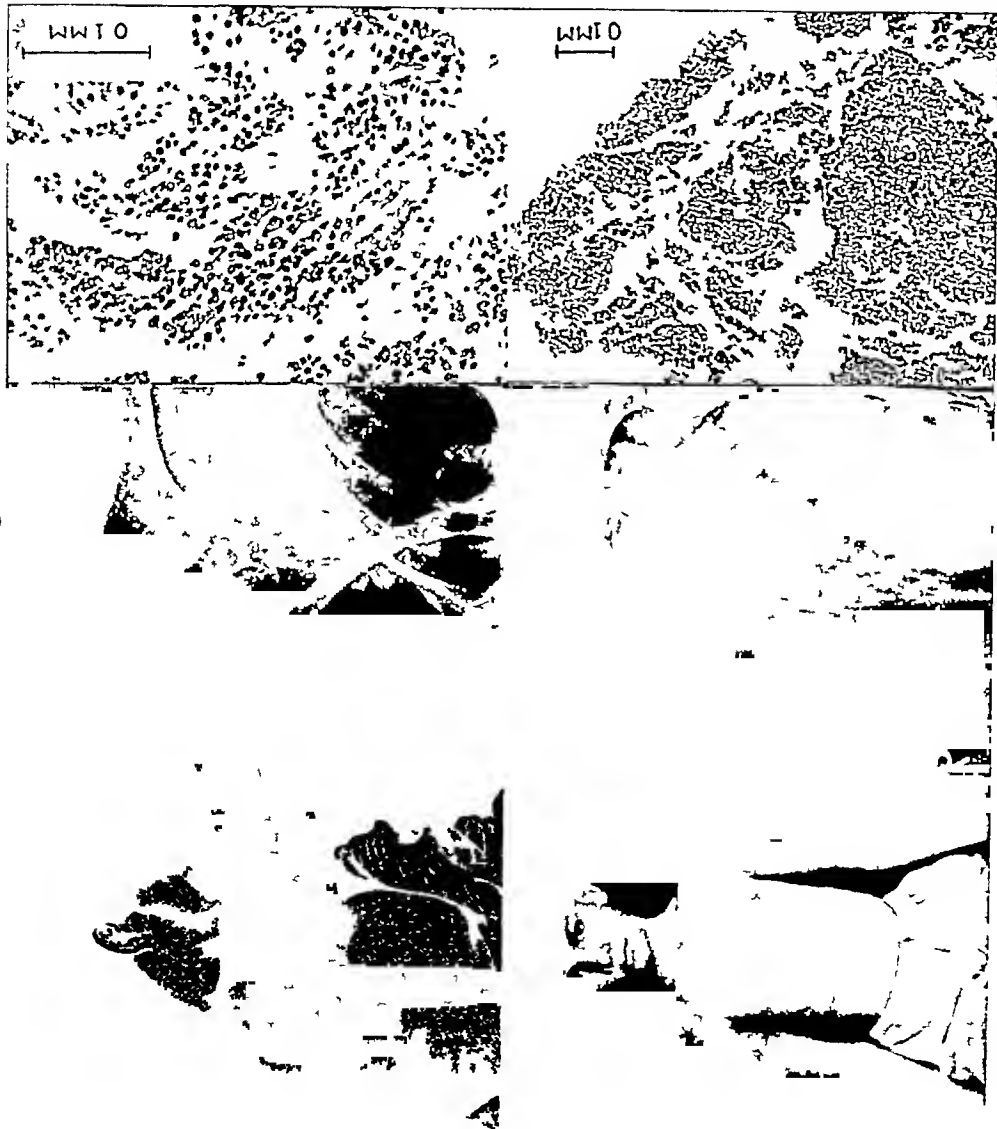
Fig 2 Skiagram showing marked destructive changes in the acromion process and in the upper border of the scapula (§ 5283)

Fig 3 Microphotograph of aspiration biopsy The tumour consists of a uniform type of cells presenting the characters of plasma cells (§ 5283)

Fig 4 Photograph showing a swelling of the size of a coconut involving the right shoulder and the upper arm (§ 5016)

Fig 5 X ray photograph showing extensive destruction, fracture of the humerus and a large tumour shadow There is some deposition of new bone (§ 5016)

Fig 6 Microphotograph of aspiration biopsy section The tumour is made up of homogeneous masses of polygonal or round cells with small hyperchromatic nuclei The nucleoli are not prominent There is hardly any intercellular material Diagnosis : Ewing's tumour (§ 5016)



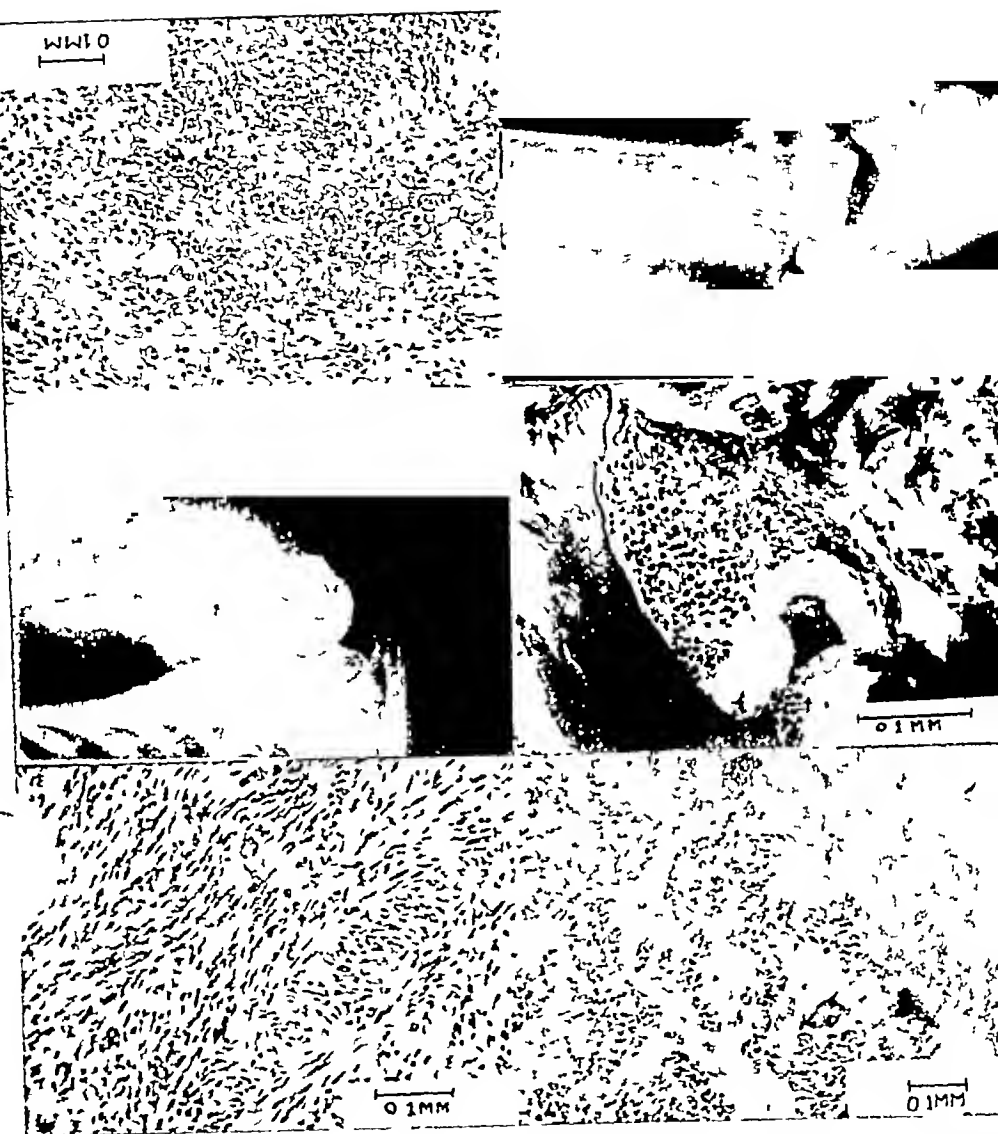


Fig. 7. Skiagram suggesting carious inflammatory changes with a small sequestrum at the upper end of the left tibia (§ 1-305).

Fig. 8. Microphotograph of an aspiration biopsy section showing splines of bone, with a small clump of cells having the characters described in Fig. 6 (§ 12302).

Fig. 9. Microphotograph of aspiration biopsy section showing clumps of large cells with clear cytoplasm, distinct outline and pale nuclei (interposed with small cells having hyperchromatic nuclei). The larger cells present unmistakable characters of cartilage cells (§ 5728).

Fig. 10. Microphotograph of tumour tissue taken from the amputated limb. The histological characters of a chondrosarcoma are very evident (§ 5728).

Fig. 11. Skiagram of the right humerus showing extensive destructive changes in the upper third of the right humerus with multiple fractures and a large soft tissue mass (§ 1440).

Fig. 12. Microphotograph showing the characteristic features of a well differentiated fibrosarcoma (§ 1-402).

a swelling began to appear which gradually increased in size. There was a dragging sensation in the arm. On examination a swelling 13 x 12 x 10 cms was found involving the right shoulder and the upper arm (Fig 4). It extended from the level of the acromial end of the right clavicle to about the middle of the shaft of the humerus. The skin over the swelling was tense and dilated veins could be seen coursing under the skin. There was a limitation of all active movements but no restriction of passive movements, except abduction.

Provisional Diagnosis Osteogenic Sarcoma of the Humerus. X-ray examination showed extensive destruction of humerus with fracture. There was some deposition of new bone (Fig 5).

Diagnosis Osteogenic Sarcoma osteolytic predominantly. Blood examination showed the following: Phosphorus—50 mgms %, Phosphatase—46 B Units, Calcium—100 mgms %, Kahn test—negative. Aspiration biopsy showed the characters of Ewing's Tumour (Fig 6). The boy was treated with x-radiation and showed very rapid regression of tumour and subsidence of pain. When he was seen a month later the condition of the arm and the movements of the limb were very good. There was no pain and there was consolidation of the fractured bone with lot of new bone formation. The examination of the chest, however, showed large mediastinal and lung metastases.

Case 3 § 12302. An 11 year old Hindu girl was brought with a suspicion of Osteogenic Sarcoma of the upper end of the left tibia by her family doctor. The patient had two or three falls while playing, without any definite history of injury at the site of the present swelling. The last of these falls was about 3 months prior to admission, and about 3 days after it the little girl began to complain of pain in the upper leg, below and on the inner side of the knee. A little later the parents noticed a swelling near the painful spot. The pain was neither severe nor persistent. It used to be felt only after walking or playing for some time. There was no pain at rest, nor was there any history of pain at night. On examination a swelling was noticed below the left knee and on the inner aspect of the leg. The swelling extended from the level of the knee to about 6 cms below it, along the shaft of the tibia. The skin over the swelling was dusky and slightly mottled due to repeated fomentations. The swelling did not feel warmer than the rest of the limb. The tenderness was moderate and was limited to the swelling. A freely movable node 2½ cms in diameter was noticed in the popliteal space three days later.

Provisional Diagnosis Osteogenic Sarcoma. The skiagrams suggested chronic osteomyelitis with a small sequestrum (Fig 7). Blood examination showed the following—Phosphorus—44 mgms %, Phosphatase (Acid)—11 units, Phosphatase (Alkaline)—19 B Units. The aspiration biopsy showed a small spicule of bone and a clump of about 25 globular cells having large round nuclei with a sprinkling of chromatin granules and a prominent nucleolus. The appearances suggested Ewing's Tumour (Fig 8). An incisional biopsy, the rapid regression of swelling and subsidence of pain during radiation therapy confirmed the histological diagnosis. She is still under treatment at the hospital. She has started complaining of

pain in the spine, in the lower dorsal region, as well as in the right chest

Case 4 § 5758 A 40 year old Hindu farmer from Belgaum was admitted for pain in the lower part of the left thigh. The pain had appeared 3 months and the swelling one month previously. There was no history of injury or a febrile illness. On examination a tumour 13x12x10 cms was found in the lower part of the left thigh. It was more prominent anteriorly, and showed markedly dilated veins over the upper part of the left shin. The tumour felt hard and its outline seemed to be merging gradually with that of the shaft of the femur. *Provisional Diagnosis* Osteogenic Sarcoma Femur. X-ray examination showed excessive new bone formation with partial destruction. *Diagnosis* Osteogenic Sarcoma. Blood examination showed the following Phosphorus—46 mgms %, Phosphatase—40 B Units, Calcium—9.4 mgms %, Kahn test—negative. Aspiration biopsy suggested the characters of a chondrosarcoma (Figs 9 and 10). The left lower limb was disarticulated at the hip and the patient made uneventful recovery. The disarticulated specimen was carefully dissected and showed the characters of a chondrosarcoma of a low grade of malignancy.

Case 5 § 12463 A 65 year old Hindu domestic servant was admitted for painful swelling of the right upper arm. The patient had noticed the swelling for the last year which had begun to grow little more rapidly during the previous three months, with occasional attacks of fever. On examination a firm globular, tense swelling at the upper end of the right humerus (diameter of about 12½ cms) was seen. Large prominent veins were visible in the skin. The movement of the shoulder was restricted probably due to the weight of the tumour. No glands were felt in the axilla. Other physical examination did not show any abnormality. Blood examination showed the following Phosphorus—39 mgms %, Phosphatase—0.5 units (Acid), Phosphatase—28 B Units (Alkaline), Calcium—7.8 mgms %, Kahn test—negative. Cytological examination—normal picture. *Diagnosis* Osteogenic Sarcoma. The radiograms showed a large soft tissue mass with extensive destruction of the upper third of the right humerus with three pathological fractures (Fig 11). *X-ray Diagnosis* Probably metastatic tumour of the bone, although a primary bone tumour could not be excluded. Aspiration biopsy showed only blood clot. An incisional biopsy showed interlacing fascicles of fusiform cells cut in different planes. The nuclei of the cells forming the bundles were ovoid, slightly hyperchromatic and a distinct nuclear membrane. The nuclei showed considerable variation in size and chromatin content. A prominent basophilic nucleolus was seen in most cells. The cytoplasm was pale and indistinct. Fine collagen fibrils were seen in and between the cytoplasmic substance (Fig 12). *Histological Diagnosis* Medullary Fibrosarcoma of the Bone. A forequarter amputation of the right limb including the scapula and the clavicle was performed. The operated specimen was dissected and showed a large (20x12x9 cms) tumour infiltrating into all the muscles covering the shoulder and enveloping the upper 1/3rd of the shaft of the humerus. The deltoid was

affected most of all and was reduced to a thin sheet of muscle fibres covering the tumour mass. The tumour was greyish white, soft and elastic. The consistency varied in different areas and the firmer portions approached the feel of hyaline cartilage. The tumour was not encapsulated. On section it was seen extending into the marrow cavity to about the middle of the shaft, with an indistinct lower margin. The upper third of the humerus was destroyed leaving a thin cone of cortical bone embedded in the tumour substance for about 4 cms. The articular cartilage covering the head of the humerus and a thin crescent of cancellous bone underneath it were unaffected by the tumour. The axillary lymph nodes were enlarged.

Case 6 § 12212 A 45 year old Muslim palace servant with a large swelling in the left hip, was admitted with the following history last month. He had noticed a small lump 5 years ago with occasional pain in the same region. He used to massage or foment the area for relief of pain. Ten months ago he had fever which lasted for two months and resulted in much loss of weight. When he got better he noticed sharp pain shooting down his leg particularly after a ride on horse back. His condition became worse and he began to feel a sense of constriction and pressure in the left foot. The tumour had been increasing in size steadily for the last 10 months. On examination a big mass was seen in the left buttock without involving the movements of the hip joint. The tumour was smooth and slightly fluctuating and faintly pulsatile. It showed enlarged veins on the surface. There was slight tenderness on pressure particularly over the sacrum. No enlargement of lymph nodes was seen. *Provisional Diagnosis* Osteogenic Sarcoma or Fibrosarcoma. X-ray examination showed a large soft tissue shadow with slight calcification in streaks. There was a complete destruction of the left lower half of the sacrum, and some destruction in its upper part. Blood examination showed the following Phosphorus—49 mgms %, Phosphatase (Acid)—0.8 units, Phosphatase (Alkaline)—2.0 B Units, Calcium—9.8 mgms %, Kahn test done on two separate occasions was negative. Aspiration biopsy showed a clump of large lipoid containing cells and inflammatory tissue. An incisional biopsy showed a very vascular pulsatile tumour. The histological examination of a piece showed striped muscle fibres separated by edematous fibrovascular connective tissue. Scattered foci of chronic inflammatory exudate mainly consisting of plasma cells and lymphocytes. The blood capillaries showed thickening of endothelial cells. There was no neoplastic tissue in the biopsy. The tumour did not show any regression with 1400 r administered in 10 days.

COMMENT

The six cases described above were selected because they illustrate the different features of the technique, and include examples of successes as well as failures. We would particularly draw the attention to the latter. Case 5 was a patient with a medullary fibrosarcoma and we believe that the architecture of the tumour consisting of sheets of spindle cells with fine wavy collagen fibrils was responsible for the inability to aspirate tumour tissue. Case 6 remains undiagnosed in spite of all our efforts. It recalls to our mind

the very sagacious observation of a master pathologist which should be remembered by all who have to deal with diagnosis of neoplastic conditions "When these data (clinical history and radiological findings) fail to give reasonable assurance the case generally remains atypical or obscure, in spite of a biopsy and throughout its course Few surgeons realise the limitations in the histological diagnosis of bone tumours and the conditions which stimulate or accompany them The sources of error are numerous" This opinion was expressed by Ewing about an incisional biopsy after an unparalleled experience in tumour interpretation

SUMMARY

A method of diagnostic technique has been described, which it is claimed obviates most of the risks attending an incisional biopsy in the case of bone tumours

APPENDIX

Histological Method Used in the Study

1 The material as soon after aspiration as possible is collected on a piece of muslin which has been spread in a petri-dish containing normal saline The dish is gently rocked to wash off the red blood cells for few seconds

2 The muslin with the material is quickly transferred to Zenker-Formol which is prepared as follows —

Solution A :	Potassium bichromate	2.5 gms
	Mercuric bichloride	50 gms
	Distilled water	1000 cc
Solution B	Neutral Formalin	

To prepare the fixative mix 9 parts of A with 1 part of B, immediately before use

3 After about 30 minutes in the fixative the small bits of tissue turn pale yellow They are then picked up and dropped in a colloidin sac containing a small quantity of fresh fixative The mouth of the sac is tied and it is immersed in a bottle containing more fixative for a couple of hours

4 Place the colloidin sac in running water overnight

5 Carry through changes of 90% alcohol, absolute alcohol and xylol

6 Embed in fresh paraffin (melting point 58 deg to 60 deg Cen)

7 Trim the block till the tissue is reached If a spicule of bone is suspected or encountered leave the paraffin block in the following decalcifying solution overnight

Ebner's Decalcifying Solution	Mercuric Chloride	0 gms
	Sodium Chloride	15 gms
	Hydrochloric acid pure	8 cc.
	Distilled water	97 cc.

8 Cut sections 5 microns thick. All sections should be mounted for study (usually about eight)

9 Stain sections in the usual way with Ehrlich's Haematoxylin and Eosin

10 Dehydrate in 95% followed by absolute alcohol, clear in xylol and mount in neutral balsam

It is a pleasure to acknowledge the assistance of our colleagues at the hospital, which has enabled us to undertake this study in the manner in which it has been presented

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Reflections and Aphorisms

True education is personal experience built up by trial and contemplation into a personal fabric of knowledge and wisdom We are taught by books and lectures We learn—that is, absorb into the fibre of our being—what we find out for ourselves, or think we do

A man who writes a book or a man who gives a public lecture is committing his reputation to cold print, or to the ears of critical strangers He must above all be accurate He cannot give expression to those half-formed ideas that are uppermost in his waking moments, to those dreams that he hopes will one day become realities and shake the world His facts are as clear-cut as the pyramids, because they have stood the test of time, his arguments are unshakable, because they have been shaken so repeatedly in the winnowing process of preparation that they have assumed a static form and a set order, his conclusions are as right as rain and about as wet Such books, such lectures, flow over our minds like water over the bed of a river, sometimes impinging on them so forcibly as to change the direction of their channel, usually doing no more than rattle the stones But it is in discussing the book with friends, in the debate of small groups before the lecture starts, or in the arguments after it is over in which the lecturer, a changed man once he has stepped from the platform, takes part, that we thrash out those beliefs that will remain with us and guide us in the years to come *It is in the sharing of inspirations yet untested, in defence or attack of theories struggling for definition, that learning is advanced and ideas are born*

The problem of self-education is one that faces each of us individually It is one that I had to face twenty years ago when I found myself standing on the high diving board of surgical registrar, secure, poorly but regularly remunerated, happy in the consciousness of honours and high degrees recently gained, and looking down on the cold and opaque waters of surgical practice into which I must now plunge How could I transform myself from a surgical oracle to whom students must listen into a wise surgeon whom doctors would wish to consult? I could never read one-hundredth of the books on the shelves or the journals on the tables, I could never

(Continued on page 138)

MITRAL STENOSIS AND PULMONARY TUBERCULOSIS

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and

P RAMAKRISHNA MUDALIAR,

Mitral stenosis and pulmonary tuberculosis is a rare combination and majority of the cardiologists and tuberculosis specialists are unanimous in this opinion. Potain and Tessier (1909) observed that they are not unusual combinations. Montenegro (1919) recorded one case of mitral stenosis in 20,000 cases of pulmonary tuberculosis. Coombs (1924) from a study of 687 cases of rheumatic heart disease

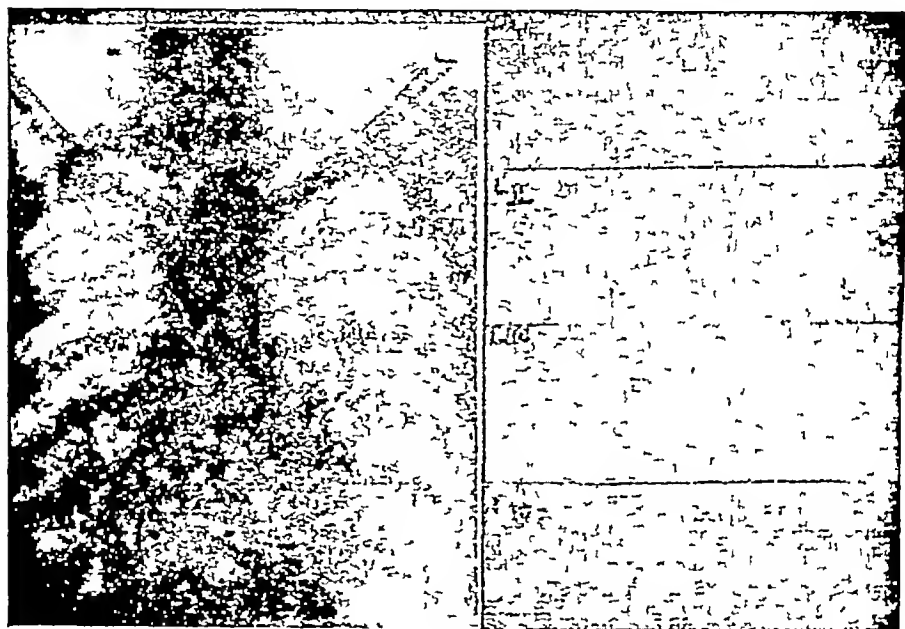


Fig 1.—Radiogram of the chest taken on 28-11-45 showing enlargement of the heart and infiltration of the lungs.

Measurements of the heart —

Right transverse diameter (in inches)	Left transverse diameter	Total transverse diameter	Transverse diameter of chest
2.40"	2.85"	5.25"	9.00"

Fig 2.—Electro-cardiogram taken on 14-12-45 Leads I, II, III and IV, F showing R. S. R. 06 per minute, P normal, L. I, L. II, L. III, indistinct in L. IV, P. R. interval 0.12 sec. T positive L. I, L. II and diphasic L. III, L. IV and right axis deviation.

did not observe even a single case and says that pulmonary tuberculosis should not be diagnosed in a patient with mitral stenosis unless the sputum shows tubercle bacilli. Buckingham and Hoffman (1935) found three cases of rheumatic heart disease in a series of 522 cases of pulmonary tuberculosis. Gloyne and Shiskin (1937) observed one case of tuberculosis in a series of 121 cases of mitral stenosis in

which the mitral valve alone was involved in 63 cases, and the rest with involvement of the aortic and tricuspid valves in addition. Paul White (1944) noted one case of pulmonary tuberculosis in 300 cases of mitral stenosis.

Tilson (1908) found old healed fibrous lesions of pulmonary tuberculosis in a few cases and Stone and Teil (1933) in 3 of the 100 post-mortems in cases of mitral stenosis.

In a series of 718 cases of rheumatic heart disease admitted into the King George Hospital, Vizagapatam, during the last 12 years (1934-45), only one case was observed in association with pulmonary tuberculosis and a brief summary of the case is given below —

L. L. N., Hindu, male, aged 18 years was admitted on 21.11.45 with a history of fever of two months and haemoptysis of four days duration. In childhood, he used to get attacks of dyspnoea while running, but there was no definite history of rheumatic joints. Eighteen months ago the patient had low fever which used to appear and disappear and lasted for six months. Four days before admission (17.11.45) he had an attack of haemoptysis and traces of blood could be seen on the 10th, 20th and 21st November.

Physical examination showed a poorly nourished individual with slight anaemia and well marked clubbing of the fingers and toes. Apex beat was seen just external to the midclavicular line in the fifth intercostal space, and the right border in the right lateral sternal line. Mitral area showed a presystolic thrill and presystolic and systolic murmurs. Systolic murmurs were heard in the aortic and tricuspid areas also. Pulmonary area showed a faint systolic murmur and an accentuated second sound. Lungs showed fine crepitations distributed all over the chest without any definite area of consolidation. Spleen and liver were just palpable below the costal margin.

A clinical diagnosis of mitral stenosis with congestion of the lungs and haemoptysis was made. Blood pressure 120/75. R B C 8 millions W B C 12,000. Poly 80% Lymph 15%, Eos. 2% and Mono 3%. Blood smear showed the picture of microcytic anaemia. Urine and motions showed nothing abnormal. Sedimentation rate was 30 mm per hour (Westergren).

The patient had a slight attack of haemoptysis while in hospital. Radiological examination on 23.11.45 showed an enlarged heart, and coarse infiltration of the lungs all over (Tubercular?) (Fig. 1). Right anterior oblique view with barium in the oesophagus did not show any enlargement of the left auricle. Examination of the sputum at first did not show any tubercle bacilli but third examination revealed the bacillus.

Electrocardiogram on 14.12.45 (Fig. 2) showed R S R₁ (96 per min.) P normal in L, I, L, II and L_{III} but indistinct in L, IV, F, P, R, O 12 sec. T positive in L, I and L, II, biphasic in L, III and L, IV and right axis deviation.

The patient was running a temperature between 99 and 102°F and had a pulse rate between 90 and 110 per minute. He was treated with a liberal diet, cod liver oil by mouth and calcium gluconate injections. A second radiogram taken on 7.1.46 showed increase in the size of the heart and more prominent pulmonary shadows. The final diagnosis was mitral stenosis and pulmonary tuberculosis, a rare combination. The patient gradually became weaker, developed cyanosis, oedema of the legs and died on 20.2.46. Post mortem was not available.

The following theories have been put forward for the rare occurrence of pulmonary tuberculosis in mitral stenosis —

- 1 The congestion of the lungs in mitral stenosis does not allow the tubercle bacilli to multiply (Coombs, Paul White, Hannesson and others)

- 2 There is a cellular or humoral immunity due to engorgement of blood in pulmonary vessels, and rheumatic diathesis is inimical to pulmonary tuberculosis (Tilson)

- 3 Pulmonary fibrosis resulting from congestion will prevent the development of tuberculosis (Gloyne and Shiskin)

- 4 Oxygen desaturation, increased CO and variation in pH of blood resulting from congestion of lungs affect the growth of tubercle bacillus (Gloyne and Shiskin)

Gloyne and Shiskin suggested that in the earlier stages there is a possibility of development of tuberculosis when there is no congestion of the lungs, but the period is too short. Fibrosis of the lungs resulting from congestion has also been ruled out by the fact that tubercular lesions in such cases must be found at the bases of the lungs but not at the apices as is usually the case. Estimation of the pH values of the blood showed 8.31 to 7.47 in cases with cyanosis to 7.4 to 7.46 in those without cyanosis.

The question whether children with healed pulmonary tuberculosis develop mitral stenosis or not has been discussed. Only few cases of healed pulmonary tuberculosis have been reported so far in association with mitral stenosis (Tilison, Stone and Teil). The incompatibility of rheumatic diathesis and pulmonary tuberculosis as suggested by Tilison might explain the same.

SUMMARY

A case of mitral stenosis with pulmonary tuberculosis is described, and the probable theories as to its rare occurrence are discussed.

Our thanks are due to Dr G. I. Benjamin for the radiograms.

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(Continued from page 135)

listen to all the lectures or visit all the great men I could only seek *self-education by co-education, by personal discussion, by learning from others what they had read and heard and imparting to them my gleanings*. I must join a surgical club. But I found that all existing clubs included surgeons of all degrees of seniority and I knew only too well the great gulf that separates men of different ages and standing, and *prohibits that almost wordless transference of mental and spiritual emanations that forms the basis of true friendship and true education*. The eminent and the humble, the professor and the pupil, belong to two worlds like Kipling's East and West, and never the twain shall meet. Pride on the one hand, guarded reserve on the other, the Jehovah complex and the inferiority complex, are seldom broken down even by good will or abolished by alcohol, the sure remover of inhibitions.

With a few friends I started a new club, the Surgical Travellers, whose aims were simple. It must be large enough to secure the respect and attention of centres we proposed to visit, but so small that all could see in an operating-theatre, all could hear at a bedside discussion, and all could discuss what they had seen and heard in the evening, the number we chose was 15. The members must represent the widest field of medical schools. And all must be of comparable standing and seniority. This little university, *for a university is an association of students for mutual benefit*, met in most of the cities of Britain and many of the capitals of Europe between the two wars. It enabled its members to grow up together, to draw strength from each other's enthusiasms, to mitigate each other's feelings. To each of us it has been a constant source of spiritual refreshment, and the affection in which we hold it to-day is an index of what we have learned from it.

—Sir Henning Ogilvie

LOCAL USE OF PENICILLIN IN OPHTHALMOLOGY

C B DHURANDHAR

It is our purpose in this paper to give our experience regarding the value of penicillin, when locally used, in some external diseases of eye. Local use of penicillin eliminates the necessity of admission to the hospital. Moreover by this method, the drug can be made available to the patient for self-administration at home.

Clinically our cases were selected under three groups

Group I Complicated and uncomplicated cases of acute conjunctivitis

Group II Complicated and uncomplicated cases of primary ulcers of Cornea

Group III Miscellaneous

1 Superficial punctate Keratitis, 3 cases

2 Chronic Dacryocystitis, 3 cases

3 Ulcerative blepharitis, 6 cases

Group I Complicated and uncomplicated cases of Acute conjunctivitis. Total number of cases investigated were 86. 78 were uncomplicated and 8 had complications (Ulcer Cornea 2, Hypopyon Ulcers 2, Angular conjunctivitis and Ulcerative blepharitis 2, superficial Keratitis 1, and descematocele 1).

Age incidence —10 between 1 and 15 years. 55 between 16 and 30 years. 21 above 30 years. *Sex* —67 were males and 19 females. *Eyes* —53 had bilateral affection. In 18 cases Right eye alone was affected and in 15 left eye. *Duration of the Disease* —Two days in 18 cases. Five days in 55 cases. More than 5 days in 13 cases.

Bacteriology —Smears of Conjunctival discharge and scrapings were examined with Gram's method, prior to treatment, for nature of infective organism. An attempt was made to note approximate number of micro-organisms in terms of +, ++, +++, (+ few, ++ some, +++ large number). Subsequently during the course of treatment the smears were examined every 24 hours until they proved to be definitely negative. In first two cases only the smears were examined every 3 hours. It was noticed that it took minimum of 24 hours for the micro-organisms to disappear completely from a smear. For want of proper facilities cultural examination could not be carried out.

Nature of Micro-organisms —The infective organisms were B Koch weeks in 37 cases. Pneumococcus 23, Gonococci 2, Morax Axenfeld diplobacillus 1, B Kochweeks, Pneumococcus and Morax Axenfeld diplobacillus 1, Pneumococcus and Morax Axenfeld dislobacillus 1. In 7 cases no micro-organisms could be detected (? allergic).

Progress of the disease —Clinically the lesions persisted for some time after the disappearance of micro-organisms from smears. Those cases only which were negative both bacteriologically as well as clinically were declared as 'Cured'.

Treatment —In first 2 cases drops of penicillin were put three hourly day and night. In the rest of the cases penicillin ointment was applied once a day to the everted lids and was continued daily.

A paper read at the 56th meeting of the G S Medical College and K E M Hospital Staff Society Bombay on February 9, 1946 with Dr S N Cooper in the chair.

until clinical cure was obtained. In cases with Corneal complications 1% atropin sulphate solution or ointment was instilled in addition to penicillin. No bandage was given.

Penicillin Solution—Solution was prepared by dissolving sodium salt of penicillin in sterilized normal saline in concentration of 2,500 units per c.c. The solution was stored in glass ampoules and was preserved in ice chest.

Penicillin Ointment—Ointment was prepared by mixing sodium salt with a base (Lanolin 1 plus Paraffin mollis albus 3) in concentration of 2,500 units per gram of base. It was stored in screw capped bottles and preserved in ice chest.

For 15 days at least neither the solution nor ointment lost its efficacy nor underwent deterioration. Because of the high cost of the drug, effect of the room temperature on the preparations could not be studied.

Untoward Symptoms—Only one case developed penicillin dermatitis which disappeared with 48 hours of stopping the drug.

Results—The results are tabulated according to the nature of infective organism. 35 cases which were irregular in attendance had to be discarded and are excluded from the tables.

Table I Acute conjunctivitis due to infection with pneumococcus, Gonococcus, B. Kochweeks, Morax Axenfeld bacillus and mixed infection (cases with Kochweeks infection alone are excluded) (See Tables I & II)

Group II Complicated and uncomplicated cases of septic ulcer of cornea, particularly with various complications like hypopyon, descematocele is a matter of considerable severity and prognosis depends upon age of the patient, general condition of the patient, nature and virulence of the infective organism and above all appropriate treatment.

Total number of cases treated were 14. 3 were uncomplicated and 11 complicated (7 Hypopyon, 3 descematocele, 1 fistula cornea). **Age incidence**—1 between 1 and 15 years, 3 between 16 and 30 years, 10 above 30 years. **Sex**—12 were males and 2 females. **Eyes**—5 cases right eye was affected and 9 cases left eye. **Duration of disease**—Less than 5 days in 8 cases. More than 5 days in 6 cases.

Nature of micro-organisms—The infective organism was Pneumococcus in 8 cases, Pneumococcus and B. Kochweeks 1, Pneumococcus and Morax Axenfeld diplobacillus 1. In 4 cases no organisms could be detected.

Progress of disease—Cases showing disappearance of ciliary congestion and formation of epithelium on the surface were considered as 'cured'.

Treatment—It consisted of instillation of penicillin ointment and 1% atropin sulphate ointment in the eye once a day only. No bandage was applied. (See Table III)

Group III Miscellaneous. Since number of cases investigated in this group is too small to draw any definite conclusion, it is proposed to continue this work further and to publish the results later.

CONCLUSIONS

As a local therapeutic agent penicillin works very well in external diseases of eye such as conjunctivitis, corneal ulcers, etc. In pneumococcal, and gonorrheal infections its action is superb. In infections with Kochweeks bacillus and morax axenfeld diplobacillus it is no way inferior to commonly used drugs. Pneumococci and gonococci disappear within 24 hours and B Kochweeks and Morax Axenfeld diplobacilli take 2 to 4 days to disappear. Clinically the condition improves within a short time.

In cases of ulcers of Cornea particularly with complication like hypopyon and descematocele penicillin far excels other therapeutic agents.

Penicillin ointment is very soothing and does not produce any bad reaction. If well-preserved the efficacy of the drug is not lost at least for 15 days.

TABLE I

Organism	Pneumococcus	Morax Axenfeld Diplo	Gonoc	Pneumo & B Kochweeks	B Kochweeks & D Morax Axenfeld	No Organism (? Allergic)
Total No	15	2	2	4	1	5
Sex	12 males 3 females	1 male 1 female	1 male 1 female	4 males	female	5 males
Eyes	Bilateral 12 R.E. 5 L.E. 8	Bilateral 2	Bilateral 2	Bilateral 3 R.E. 1	Bilateral	Bilateral 2 R.E. 2 L.E. 1
Duration of disease	3 cases 2 days 6 cases 5 days 6 cases more than 5 days	1—4 days 1—3 months	1—4 days 1—6 days	4—4 days	20 days	4—2 days 1—5 days
Uncomplicated	11		1	4	1	5
Complicated	4 2 Ulcer Cornea 2 Hyp Ulc Cor	2 1 Superficial Punctate Keratitis with tiny Ulcer Cornea 1 Ulcer Blepharitis.	1 B.E. Descematocele			
Age Incidence	4-1 & 15 3 16 & 30 3 above 30	1 1 15 1 above 30	1 11 years 1 30 years	1-1 15 2-15-30 1 above 30	1 1 15 Angular Conj & Ulc blepharitis	1 1 15 3-16-30 1 above 30
Disappearance of organism	14 cases with 1 in 24 hours 1 case 48 hrs	1 in 1 day 1 in 3 days	Both 24 hrs	Pneumo 3 in 1 day 1 in 2 days Koch 1 in 2 days 3 in 3 days	Koch 1 day Morax 2 days	
Clinical cure	2 in 2 days 11 in 4 days *1 in 6 days †1 in 10 days	1 in 4 days 1 in 5 days	1 in 6 days 1 in 17 days	3 in 5 days 1 in 6 days	5 days	3 in 2 days 2 in 4 days

Remarks —*This was a case of hypopyon Ulcer Patient was an old woman Ulcer healed but hypopyon did not disappear In this case pupil could not be dilated †In this case Organism wases ++ and Patient was irregular

(1) In uncomplicated case penicillin drops were used hourly for first 2 days & next 2 days 3 hourly
(2) In complicated case for first 3 days ointment was used 3 hourly Next 14 days it was used T.D.S. Internally sulphadiazine was given This is an interesting case Patient came with both cornea practically destroyed & vision was P.L. only On 6th day vision became finger counting 1 foot On 17th day B.E. F.C. 3 feet

Since no organisms were detected 3 cases were treated: 1 penicillin ointment and 2 with 2% silver nitrate solution Cases with penicillin treatment recovered in 2 days whereas those with silver nitrate took 4 days.

TABLE II

Acute Conjunctivitis due to B. Kochweeks infection Since it was found that B. Kochweek was not quite non resistant to penicillin some cases were treated with 2% Silver nitrate solution and some with sulphamamide ointment. Unfortunately in this group good many cases had to be discarded due to irregular attendance

Treatment	Penicillin	2% Silver Nitrate solution application	2% Cibazol Ointment
Total number	6	10	0
Sex	Male 6 cases	Male 8 cases Female 2 cases	Male 8 cases Female 3 cases
Eyes	R.E. 2 cases L.E. 1 case Both Eyes 3 cases	L.E. 1 case Both Eyes 9 cases	R.E. 1 case Both Eyes 5 cases
Duration of Disease	1 case 2 days 4 cases 5 days 1 case more than 5 days.	4 cases 2 days 5 cases 5 days 1 case 1 day	4 cases 2 days 2 cases 5 days
Uncomplicated	0	10	0
Complicated	Nil	Nil	Nil
Disappearance of Micro-organism	5 cases 2 to 4 days 1 case 6 days	10 cases 2 to 4 days	
Clinical Cure	1 case 6 days 3 cases 7 days. 2 cases 8 days	0 cases 7 days 1 case 8 days	
Remarks —			These cases would not respond to Cibazol and hence were treated with silver nitrate solution and got cured

TABLE III

Uncomplicated and complicated cases of primary ulcers of cornea

	Uncomplicated.		Complicated	
	Pure Ulcers.	Hypopyon ulcers	Descemetocoele.	Fistula cornea
Total number	3	7	3	1
Sex Incidence	Males 3	Males 6 Female 1	Males 3	Male 1
Age Incidence	2 Bet. 10 & 30 1 above 30 yrs.	1 Bet. 10 & 30 6 above 30	1 Bet. 1 & 15 2 above 30	1 above 30
Eyes	R.E. 2. L.E. 1	R.F. 1 L.E. 0	R.E. 1 L.E. 2	R.E. 1

Duration of Disease	5 days 3	5 days 4 more than 5 days 3	Within 5 days 1 more than 5 days 2	More than 5 days 1
Organism	Pneumoco 1 No organism 2	Pneumo 5 †Pneumo & B Koch 1 Pneumo & Morax Anxe 1	Pneumo 2 No organism 1	Pneumococcus 1
Disappearance of Organism	24 hours.	Pneumo 3 cases 1 day 8 cases 2 days Morax 1 day	24 hours	24 hours
Clinical Cure	2 cases 8 days *1 case 15 days.	1 case 2 days 1 case 3 days 1 case 4 days 3 cases 5 days 1 case 6 days	1 case 9 days 1 case 11 days 1 case 15 days.	17 days.
Remarks.—	*In this case ulcer was very deep. The organism could not be detected.	†This case with Pneumo & Koch weeks infection did not respond	These cases are worth noting. Usually desecma tocele means perforation of ulcer and blindness	Anterior chamber was reformed

DISCUSSION:

Dr S G Joshi asked whether the lacrimal sacs rendered sterile by syringing with Penicillin solution would remain permanently sterile. He also enquired whether the drug in the form of solution or ointment was preferable.

Dr A S Paranjpe said that the Penicillin was active against Gram positive organisms and relatively feeble against Gram negative organisms except the *Nesseria* group. He observed that in the series presented it was interesting to note that infections produced by *Kochweeks* and *Morax Axenfeld* bacilli were controlled by Penicillin. He wanted to know the characteristics of atypical penicillin dermatitis referred by the speaker as occurring in one of his cases.

Dr S N Cooper wanted to know whether there were any failures in the treatment with Penicillin and also the way the ointment was rendered sterile.

Dr A V Baliga enquired whether penicillin could be used as a prophylactic to prevent neuro-paralytic keratitis following destruction of the Gasserian ganglion.

Replying to Dr Joshi, Dr Dhurandhar said that the number of cases observed by him was small and the cases were not under continuous observation and henceforth the lacrimal sacs would be observed as the work was being pursued further. He continued that the ointment was better than the solution as it was more soothing, remained longer in the eye and its effects lasted for a longer time.

In reply to Dr Paranjpe, he said that in case of dermatitis the eyelids were red and hot and it was the Dermatologists' opinion that it was due to Penicillin. He further added that clinically Penicillin was found to be effective in infection produced by *Kochweeks* and *Morax Axenfeld* Bacilli.

Replying to Dr Cooper about the preparation of the ointment, he said that the base was at first boiled and cooled and then the penicillin powder was mixed with it in a sterile vessel. With regard to failures in the treatment, he observed that in two advanced cases there was no improvement after the use of Penicillin and in these cases treatment by other means had also failed.

In reply to Dr Baliga, the speaker was of the opinion that the ointment could be used as a prophylactic, in the same way that it was used after the operation for alighting the cornea for corneal opacity.

Dr S N Cooper in his concluding remarks said 'It is apparent that Penicillin treatment in ophthalmology presents problems very different to those when the same drug is administered parentally in affections of the other parts of the body. It is easy for Penicillin to reach the external surface of the eye and to obtain a saturation of 0.1% penicillin per c.c. of serum required to produce bacteriostasis in the case of staphylo-aureus and 0.01% per c.c. of serum in the case of *Streptococcus* lyticus a few drops of as weak a solution as 250 units of penicillin per c.c. are needed.

Here the problem was as to the best way of applying the drug locally whether by way of an ointment or by way of drops. Dr Dhurandhar has been using the ointment successfully, but as far as the base of the ointment is concerned I may suggest that has been recommended in the literature that 8 parts lanette wax when mixed with 7 parts of distilled water, provides a good cream for preparing the ointment. The base can be autoclaved at 120°C, and penicillin solution added when it cools to 60°C.

When Penicillin is to be tried for deeper or intraocular sepsis various new problems arise. The drug can be administered locally by way of drops, bath or ointment or by iontophoresis or by subconjunctival injections or parenterally. Parenterally it is proved to be useless because the quantity of penicillin thus recovered from the anterior chamber and vitreous is not sufficient to produce bacteriostasis. Iontophoresis and subconjunctival injections have much to recommend them, especially the latter because in this way a single injection of 1 c.c. of a 1000 units per c.c. solution is supposed to find its way to the anterior chamber and vitreous and remain there in a bacteriostatic concentration for 24 hours.

However topical applications are useful even in deeper sepsis, for I can recall a case where on the day after a successful cataract operation on a lady, the anterior chamber became full of pus with a small pustule on the iris. The wound was perfectly healthy and evidently this was sepsis by metastasis. Penicillin drops locally and Penicillin parenterally brought about a rapid absorption of pus. About 10 days later pus appeared again in the anterior chamber. This time, only drops, of Penicillin were put in the eye, which brought about complete resolution of the pus, very soon, proving the beneficial effects of local use of penicillin even in deeper sepsis.

The other problems in intra-ocular sepsis that may be considered will be the comparison of effects of Penicillin when the corneal epithelium is intact and when not intact and the effects of Penicillin in the presence of ruptured globe.

Critical Notes and Abstracts

ADVANCES IN VITAMIN THERAPY

Research in the vitamin field has been undergoing a gradual change in the last few years—a change which has broadened its scope until it now extends far into the field of biochemistry. The line dividing vitamins from essential amino acids has been broken down so completely by the newer concepts and conclusions that it can hardly be said to exist. This change is reflected in the vitamin literature of the past year.

Hepatic Cirrhosis

Recent publications have increasingly stimulated the clinical interest in dietary management of cirrhosis. From a limited number of cases Russakoff and Blumberg felt that the use of *choline* is justifiable as an adjuvant to dietary therapy of cirrhosis of the liver, particularly of the fatty "alcoholic" type. In six instances, a diet high in protein and carbohydrates, and low in fat supplemented by vitamin B complex was tried for several weeks without benefit. Within a week after the addition of *choline chloride*, obvious responses were noted in three of the cases and probable responses were subsequently observed in two of the other patients.

Rimmerman *et al* studied ten patients having cirrhosis without jaundice. Subjective and objective improvement, as measured by results of liver function tests, were observed when a similar diet was supplemented with choline in the form of *lecithin* for a period of six to sixteen weeks. Treatment of fatty liver and cirrhosis by a dietary regimen, supplemented with 15 Gm of choline chloride daily, was considered by Barker to be the most promising form of therapy for this disease, even after signs of hepatic decompensation such as jaundice, ascites and hematemesis have developed.

Wade pointed out that clinical and experimental data suggest, but do not prove, that human cirrhosis is primarily a nutritional disease. Early fat deposition in the liver is accompanied by anorexia, which in turn results in a severe malnutrition. For the treatment of cirrhosis he advocates (1) the immediate elimination of any etiologic agent, (2) reduction in the amount of dietary fat available to the liver, (3) assistance in the mobilization of liver fat by use of lipotropic factors, such as *choline chloride*, 1 to 2 Gm daily, and *methionine* as contained in milk, and (4) provision of a diet adequate in all known dietary essentials. He stresses the importance of early diagnosis of cirrhosis since moribund patients with profound liver destruction are obviously beyond the help of any conceivable therapeutic procedure. Jolliffe and Alper obtained favourable results in treatment of cirrhosis by the use of a high protein, high carbohydrate, moderate-to low-fat diet, plus fortified casein hydrolysates, dried brewer's yeast, parenteral liver extract and administration of specific vitamins when they are indicated. The various lipotropic factors—casein hydrolysate, choline and methionine—may be used experimentally either alone or in combination.

Progressive Anacmia

In a case of *Addison-Biemer's disease* which developed a pro-

gressive anemic state under treatment with adequate amounts of purified liver extracts, Moosnick *et al*, reported that the anemic state responded well to the intravenous administration of 1 Gm choline chloride daily for sixteen days. A fatty state of the liver and bone marrow tissues was believed to have been the reason for the failure of the patient to maintain a normal blood status. Richardson and Suffern found no therapeutic value in daily administration of 15 Gm of choline chloride to sixteen cases of infective hepatitis. The diet taken was low in fat and high in carbohydrates. The protein intake was not checked.

Hepatorenal Failure

One case of severe hepatorenal failure treated with intravenous choline chloride followed by methionine was reported by Barclay and Cooke to have resulted in successful recovery. *Choline* was administered first (5 Gm orally, followed the same day by 2 Gm in dextrose and saline solution). Eight grams of choline were given by the intravenous drip method on each of the next two days. On the fourth day, 6 Gm of choline and 4 Gm of methionine were administered by intravenous drip. *Methionine* alone was given on the fourteenth day of this course of treatment. The author felt it was justifiable to conclude that choline was the casual factor in the restoration of kidney and liver function, which started within twelve hours after administration of choline was begun. Because of the suggestion that choline brings about retardation in erythropoiesis, Cartwright and Wintrobe gave choline chloride to three adult males in daily oral doses of 30 mg per kg of body weight for ninety days. Neither anaemia nor macrocytosis occurred in any patient.

Bio-synthesis of Vitamins

Recognition of the ability of intestinal bacteria to synthesize vitamins has directed attention to the question of availability of the biosynthesized vitamins for human nutrition. The work of Najjar and Holt in which severe deprivation of thiamine was required to produce signs of thiamine deficiency has been generally interpreted to indicate that bacterial synthesis of thiamine may play an important role in thiamine nutrition. The hypothesis that thiamine was absorbed from the large intestines was supported by the finding that a retention enema containing the vitamin increased the urinary excretion of thiamine. The validity of this work was challenged by Alexander and Landwehr. The availability of thiamine and cocarboxylase produced by intestinal flora was questioned since they appeared to exist largely within the bodies of bacteria. This was concluded from the observation that removal of organisms from a water suspension of feces resulted in a marked decrease in the thiamine present. Alexander and Landwehr pointed out that the two successive 50-mg retention enemas used by Najjar and Holt constituted a huge dose as compared with the amounts normally present in human feces. Furthermore, most of the thiamine in feces is in the form of cocarboxylase, whereas, in the experiment, only free thiamine was administered to the subjects of the study. A thiamine retention enema, containing twice the amount of free and phosphorylated thiamine usually present in fecal matter was administered. No increase in the urinary thiamine excre-

tion was noted

In reviewing the studies, the *British Medical Journal* called attention to the observation of Grant *et al*, that some 40 percent of the vitamins synthesized by bacteria can be extracted from the cells by aqueous media. The conclusion was that the subject requires further investigation. *Nutrition Reviews* concluded that even though the utilization of fecal thiamine may be very limited and can hardly be regarded as being the cause of serious errors in determining dietary requirements, it cannot be denied that sufficient amounts may be absorbed during severe restrictions to prolong the onset of deficiency symptoms.

Interrelation of Vitamin Activity

Richard's recent experimental work has renewed interest in the possibility of interrelation of vitamin activity. In reviewing the literature, the author acknowledges the fact that in many cases the deficiencies are multiple and that treatment of the predominant deficiency with a single factor of the vitamin B complex shows up other deficiencies which have previously been masked. The possibility is considered that, in some cases at least, secondary deficiencies may be induced by excessive dosing with one factor and may give rise to a deficiency which was not present under the original condition. In her experimental work the author demonstrates that overloading the diets of rats on a diet low in pyridoxine with large amounts of thiamine causes vitamin imbalance with the consequent production of pyridoxine deficiency. Therefore, she emphasizes the need for caution in any attempt to improve clinical diets by the indiscriminate addition of large supplements of single factors of the vitamin B complex factors.

Previously Klopp *et al* had observed in many instances a transitory increased excretion of riboflavin following administration of thiamine to human beings. However, it was not possible to induce either clinical or chemical evidence of riboflavin deficiency in these individuals by the daily administration of large amounts of thiamine for as long as a period of 73 days. From their studies of thiamine deficient patients, Ferrebee and Weissman conclude that thiamine deficiency is not of clinical significance in the production of riboflavin deficiency. Changes in riboflavin metabolism were observed only in the terminal stages of thiamine deficiency and appeared to be unspecific and of minor importance. In a comparison of intravenous and oral vitamin tolerance tests made with sixteen subjects, Johnson *et al* found that any combination of two of the factors, thiamine, riboflavin and ascorbic acid, could be administered without affecting the urinary excretion of other vitamins. Nicotinamide alone had no effect on the excretion of the other three factors. Ghalloungui and Jallily commented that the constant association of all members of the vitamin B group may not be a chance occurrence but that they are interdependent and deficiency of one may lead to a deficiency of others. In the same way, if each had a role in succession in a long metabolic process, failure at any stage would lead to the same end-result. In view of the possibility of vitamin imbalance, the *Journal of the American Medical Association* has commented that balancing of vitamins may

be of a considerably greater clinical importance than has been thought

Hemolytic Disease of the Newborn

In cases of hemolytic disease of the newborn, Leonard proposes the administration of *vitamin K* to Rh-negative donors before withdrawal of blood. Kinsey had previously noted remarkable control of bleeding tendencies in cases of *acute yellow atrophy of the liver* when the patients were given transfusions from donors who had received *vitamin K*.

Beriberi complicating established heart disease

The diagnosis of beriberi heart ten times in a period of four years has led Blankenhorn to believe that the disease is not rare in hospitals where other deficiency diseases occur, and that beriberi may complicate chronic heart disease of other etiology. The following criteria for the diagnosis of beriberi heart disease were proposed: (1) enlarged heart with normal rhythm (sino-auricular), (2) dependent edema, (3) elevated venous pressure, (4) peripheral neuritis or pellagra, (5) nonspecific changes in electrocardiogram, (6) no other cause evident, (7) gross deficiency of diet for three months, and (8) improvement and reduction of heart size after specific treatment, or autopsy findings consistent with beriberi.

Painful Postpartum Nipples

Preliminary evaluation by Brougher of a *vitamin A and D ointment* in preventing and treating painful and tender postpartum nipples, indicates that results with the vitamin ointment are far better than with other methods.

Glossitis and Cheilosis and Burning sensations in hands and feet

Calcium pantothenate caused complete healing or good progress after administration of other factors of the *vitamin B complex* had failed in six cases of glossitis and one of cheilosis which were observed and reported by Field *et al*. Calcium pantothenate has been successful in relieving burning sensations in palms and soles, where other measures have failed.

Nicotinic Acid in Confusional States

The results from use of massive doses of nicotinic acid in the treatment of a post-traumatic *confusional state* suggested to Lehmann therapeutic possibilities in traumatic psychoses. Seven weeks after the accident the patient was administered 800 mg of nicotinic acid daily for one week. Memory and orientation rapidly improved after the second day, the convalescence was uneventful.

Senile psychosis was shown to be simulated by pellagrous encephalopathy in two cases reported by Meyersburg. The senile-pellagrous psychosis responded well to treatment with crystalline *vitamin B complex* factors and natural *vitamin B concentrates*. It was advocated that elderly persons should have diets of *optimal rather than minimum adequacy*. When the maintenance of an adequate diet becomes impractical, dietary supplements should be administered.

Folic Acid in Leukopenia, Macrocytic Anaemia and Sprue

By intravenous administration of liver concentrate containing *folic acid* to seventeen nutritionally deficient patients with leukopenia,

Berry *et al* found that in thirteen cases this treatment elevated the total number of leukocytes with a proportionate increase in granulocytes, for varying periods. When this change occurred, it was accompanied by a left shift. Crystalline *L casei* factor ("follic acid") administered intravenously to five patients early in the morning was followed by some rise in leukocyte count of the peripheral blood later in the day. This elevation was maintained on the following day in only one case. By footnote, Berry and Spies mentioned administering to ten malnourished persons with leukopenia, a white, colorless material, chemically different from *L casei* factor, which was isolated while fractionating a purified liver extract. The rise in white cell concentration of the peripheral blood was spectacular. *L casei* factor concentrate was given orally to seventeen cases of refractory anemia or leukopenia by Watson *et al*. No effect was observed in the eight cases of refractory anemia, nor in one case of leukopenia persisting after sulfonamide therapy. In each of six cases with leukopenia resulting from local intensive Roentgen-ray therapy, elevations in leukocyte count were noted. Elevation was also noted in one case of polycythemia vera receiving total body radiation. No effect was observed in one case of Hodgkin's disease exhibiting severe leukopenia following intensive Roentgen-ray therapy. Because of these results, the authors suggested further investigation and study of the possible effectiveness of "follic acid" in the treatment of certain types of leukopenia.

There has been another direction in which follic acid has become a substance of great interest. Its crystallization led to its identification with vitamin B₁₂—an anti-anaemia factor for the chick. The outcome of the indication that follic acid was concerned not only with the production of the white cell in the bone-marrow but also with the production of the red cell is that Spies has recently described the successful treatment of macrocytic anaemia with follic acid. Spies has been working in the southern part of the United States at a centre he established in Alabama, where severe malnutrition is still relatively common. As far back as 1930 he observed that many with pellagra suffered from a macrocytic anaemia exactly like a pernicious anaemia, except that there was no achlorhydria. This nutritional macrocytic anaemia was not due to lack of Castle's intrinsic factor, for the gastric juice of these patients, when incubated with meat, caused a reticulocytosis in patients with pernicious anaemia. Spies therefore began, at Birmingham in Alabama, to hunt for the missing nutritional factor. After the identification of follic acid with the anti-anaemia factor in the chick, Spies must obviously have had a keen interest in supplies of follic acid. But its extraction from liver, yeast, and other sources results in a poor yield, and only its synthesis could make possible sufficient supplies for testing. In August 1945, the synthesis of follic acid (*L casei* factor) was announced by sixteen investigators (Angier *et al*). The following month Spies, Vilter, Koch, and Caldwell reported the results of the first clinical use of synthetic follic acid in the treatment of macrocytic anaemia. The results are that out of 42 cases of macrocytic anaemia 26 responded to an administration of follic acid, and of these five were patients with Addisonian

pernicious anaemia This effect of folic acid in pernicious anaemia is of the greatest interest, and suggests that the position of Castle's intrinsic and extrinsic factors will require reconsideration Among the other patients successfully treated were 8 with sprue, in whom not only did the anaemia disappear but the liquid fatty stools turned to solid brown faeces

Spies has further reported on the effect of folic acid on persons with macrocytic anaemia in relapse 41 of the 45 patients had typical macrocytic hyperchronic anaemia and 4 had iron deficiency anaemia with a low colour index Of the 41, 8 were cases of nutritional macrocytic anaemia, 8 pernicious anaemia, 11 sprue, 3 pregnancy anaemia, 1 associated with carcinoma, 1 cirrhosis of liver, 3 undetermined origin, 3 aplastic anaemia, 3 leukaemia Of these 7 patients had pellagrous symptoms Folic acid was administered orally 20 mg or more a day, or parenterally 5 to 30 mg, a soluble salt being prepared by adding a normal sodium bicarbonate solution Prompt improvement occurred in the general condition and in the blood condition of 26 of the 27 patients in 3 to 8 days In patients with aplastic anaemia, leukaemia, and iron deficiency, no improvement could be detected either clinically or by means of laboratory examinations Spies writes that after the use of folic acid, there is a tremendous upsurge of well-being, an increase in strength and vigor, a return of appetite and a desire to walk about Folic acid, a vitamin present in liver, yeast and other food materials, (synthetic *Lactobacillus casei* factor), is a potent *antianaemia factor* in certain types of macrocytic anaemia in relapse Folic acid performs a specific function in the maturation of the various cells of the bone marrow and has other obvious profound effects on our bodies

Pyridoxine in Agranulocytic Angina

Three cases of *agranulocytic angina* successfully treated with pyridoxine hydrochloride were reported by Cántor and Scott In these cases, sulfathiazole, acetylsalicylic acid, and phenobarbital and thiouracil respectively, were ingested prior to the development of the typical clinical and hematological features of *agranulocytic angina* Pyridoxine was administered in doses of 200 mg intravenously, daily

Vitamin E in Nephrosis

In a few case histories presented by Shute, it was indicated that treatment with vitamin E may improve damaged kidney function The improvement developed quickly, but was transient unless the therapy was continued, and was apparently limited to the tubular system of the kidney The results from a case of true nephrosis suggested that vitamin E therapy may play a role in the management of this disorder Nicotinic acid in large doses is useful in relieving eye symptoms in nephritis

Menopause

The clinical use of vitamin E in the treatment of menopausal symptoms was described in a preliminary report by Christy The relief of symptoms in patients after administration of vitamin E could not be distinguished from that obtained with estrogens In some cases vitamin E seemed more effective in relieving the symptoms of

vasomotor instability than estrogens. The vitamin produced no untoward after-effects.

Wernicke superior encephalitis

Thiamine and vitamin B complex therapy effected complete or almost complete cure in three cases of superior encephalitis of the Wernicke type reported by Kravitz and Stockfish. There was no history of alcoholism in any of the cases, and features of vitamin B complex deficiency such as cheilosis and glossitis were observed in only one case.

Urticaria

After administration of synthetic *menadione* (vitamin K), improvement was observed by Black in 62 per cent of 156 cases of urticaria in which the usual methods of treatment had failed. The duration of treatment varied from one to four weeks. In many instances, lesions failed to appear after two days of treatment, and of those relieved, 75 per cent were free from lesions within one week. Relapses followed asymptomatic periods which varied from two weeks to eight months. Readministration of the vitamin brought about prompt relief in each instance. No second recurrences were observed.

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Original Contributions

PENICILLIN IN ACUTE NEPHRITIS

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The therapeutic use of penicillin has become the method of choice in the treatment of acute coccal infective conditions Fleming (1929), Heilman and Harrell (1942) proved conclusively its antibacterial action against a wide variety of pathogenic organisms Herrell, Heilman and Williams (1942), Keefer, Blake et al (1943), Harrell (1943) have demonstrated its use in the treatment of a large number of clinical conditions in men

It has been suggested that penicillin is theoretically indicated in the treatment of acute nephritis, but no series of cases so treated has yet been published

The pathogenesis of acute nephritis lies in a primary infective process, however insignificant, situated in the oral cavity, nasopharynx, alimentary, respiratory or genito-urinary systems Secondary to this 'septic focus', a progressive recurrent renal inflammation is set up We find in the nephritic kidney all the fundamental features of inflammation, viz, exudation, proliferation and degeneration Proliferation, which is most in evidence in the earlier phases, is seen in the tuft epithelium and in the endothelium of capillaries, the glomerulus becomes relatively avascular and an exudate rich in polymorpho-nuclear leucocytes appears The swollen epithelium is shed and the space between the layers of Bowman's capsule as well as the whole interstitial kidney substance is filled with an exudate containing coagulated albumin, fibrin, white and red blood cells

The primary infective process, therefore, is directly responsible for the nephritis, and as long as it remains there is a tendency to repeated acute or subacute exacerbations in the renal inflammation If the primary focus is definitely localised to an infected tonsil or tooth, it can be removed, but in most cases it is not so easily localised or eliminated Also, the focus is very often streptococcal, sometimes haemolytic, and knowing the extreme susceptibility of these organisms to the sulphonamide group of drugs one is tempted to use them when local or surgical elimination is not possible Evidence is accumulating, however, that even healthy kidneys do not tolerate the

'Sulfa' group of drugs well as shown by cases of anuria and haematuria with Sulfadiazine and Healey (1946)) reports anuria with Sulphapyridine

Herrell, Nichols and Heilman (1944) and Bloomfield, Rantz & Kirby (1944) have extensively reported the use of penicillin in the treatment of various clinical conditions and they stress the fact of its being completely devoid of any toxic effects on the kidneys Chain, Florey and co-workers (1940) have shown the absence of toxicity of penicillin for most other tissues and Herrell, Nichols and Heilman (1944) have shown the complete absence of toxic disturbance in the haemopoietic system or peripheral blood Unlike the 'Sulfa' drugs, penicillin has been used successfully in the presence of severe anaemia, leucopenia or even, as recorded, of agranulocytosis

In acute nephritis where the primary focus is of infective origin and signs and symptoms of inflammation are present, local and constitutional, it is reasonable to expect that if the primary focus is eliminated the kidneys have a better chance of remaining free from repeated exacerbations and consequent progressive degeneration Penicillin, with its complete absence of toxic effects on the kidneys, is the obvious drug of choice, specially in view of the inflamed condition of the kidneys and the presence of impaired renal function where the question of drug toxicity assumes a magnified importance In fact, according to Morgan, Christie and Roxburgh (1944) a higher blood concentration may be maintained with a comparatively smaller dosage in such cases

CHOICE OF CASES

In this series 25 patients, 10 being under 4 years of age were treated Almost all were in critical condition, in some life was despaired of, and some were chosen for their complete failure to respond to any other form of treatment In some, a primary infective process was demonstrable and the leucocytic count was raised Rise of temperature was present in 15 and in some of them oliguria or complete anuria had set in with variable amount of oedema One child had severe haematuria The last 10 cases of the series have been grouped together because they were all afebrile, or nearly so, and their chief trouble was oliguria or anuria with oedema

METHOD OF ADMINISTRATION AND DOSAGE

100,000 units of Penicillin were dissolved in 20 ccs double distilled water, except in the case of very young patients where 10 ccs were used in order to make each injection as small as possible in bulk In these, normal saline was used as solvent The solution was kept constantly cooled and all injections were given intramuscularly, avoiding leakage into oedematous subcutaneous tissues

The dose per injection varied between 5000 and 15000 units, administered at 3 hourly or in some cases at 4 hourly intervals The total dosage, in any one course varied between 168,000 and 64,000 units, except in Case nos 6 and 19 who died early in treatment

DISCUSSION

Penicillin in acute nephritis seems to act in two distinct ways. One, where there is evidence of a primary infective focus it acts as a strong bactericidal agent and removes or eliminates the source of infection Garrod (1945), and secondly it is conceivable that it acts on the inflammatory exudate in the renal substance and relieves the congestion and mechanical pressure on the glomeruli and uriniferous tubules, i.e. the nephrons are, in effect, mechanically decompressed and allowed to resume the work of excretion, secretion and reabsorption which constitute their normal function.

Of the first 15 cases of this series which were febrile and acute infection was present, those that were not complicated by marked oliguria or anuria showed remarkable improvement. The temperature dropped to normal in 36 to 72 hours, the urine output increased appreciably and it became free from abnormal constituents. In the other febrile cases where the most marked feature was anuria, extreme oedema or general anasarca, improvement was first registered by lowering of temperature due to control of the infective process and the oedema gradually diminished following the increased urinary output.

The 10 nonfebrile cases, where the most marked feature was generalised oedema showed a rapid increase in urinary output and relief of symptoms in response to penicillin, thus confirming what has been postulated above regarding the action of this drug on the removal of inflammatory exudate from the kidney substance.

Case no. 6 was very toxic from the start and had severe haematuria, possibly as a complication of intensive Sulfadiazine treatment given before admission. Case no. 19 showed no response to treatment.

A most marked feature of penicillin treatment in this condition is the greatly reduced time of treatment, which varied from 3 to 8 days in this series as compared to the weeks or months taken by usual conservative methods.

There is no doubt, therefore, that penicillin has a definite place in the treatment of acute nephritis, by way of arresting or eliminating the primary infective process, by controlling or combating the inflammatory changes in the kidney substance, and by the absolute reduction in the time of treatment required.

It may be mentioned that no toxic complications due to the use of the drug were noted in this series, and the word "recovered" used in the table* of cases implies relief or freedom from symptoms and does not necessarily imply a permanent cure.

SUMMARY

25 cases of acute nephritis, some of them in very critical condition, received systemic penicillin treatment.

* Dr Sen has submitted a long table summarising the clinical features and details of treatment of the 25 cases which for reasons of space it is not possible to print. Most of the pertinent information is summarised in the article.—*Editor*

The total absence of toxicity to renal and other tissues and the bactericidal action of penicillin is exploited to remove the causal infective process

There is clinical evidence to believe that penicillin probably relieves the inflammatory congestion and exudation in the kidney substance, thereby improving the impaired renal function and increasing the output of urine, as shown by its action in the nonfebrile oedematous cases

The duration of treatment is greatly reduced as compared to that taken by other conservative methods to tide over and bring under control an acute attack

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CIRCULATORY FAILURE AND ITS TREATMENT

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A study of old scripts and writings by Egyptologists has revealed the amazing fact that a study of the heart and circulation began as far back as three thousand years before Christ Hieroglyphics or primitive signs depicting the heart and circulation have been discovered in the Edwin Smith papyrus The central action of the heart in the maintenance of the circulation was described for the first time in England by Harvey Though the essential conception of circulatory dynamics has remained unchanged to this day, we attach a lot of importance nowadays to arterioles and capillaries in the maintenance and normal functioning of the circulation

The word "*Compensation*" was first introduced to medical nomenclature about seventy years ago by Traube, it is a highly useful addition to medical vocabulary, it has made possible our present-day concept of heart disease in terms of compensation and decompensation Compensation represents the various mechanisms employed by the body in an attempt at neutralizing or correcting adverse influences and impediments to normal body-phenomena In the case of the heart, valvular, myocardial and coronary disorders, though capable of a pronounced influence on the circulation, are kept in check, often for long periods of time, by the phenomenon of compensation Examples of this abound in everyday life, we see middle-aged men with severe and long-standing hypertension engaged in occupations entailing considerable mental and physical effort, they are frequently the head-men in big business organizations, some hypertensives are even working as dock labourers and farmers A Bombay doctor has been managing a "roaring practice" in spite of a blood pressure of over 230 m.m systolic Valvular lesions, like aortic regurgitation and Fallot's tetralogy, are sometimes discovered on routine medical inspection in children, who have indulged in strenuous games and exercises all their lives

In diseases of the cardio-vascular system, the real danger lies in lack of nutrition or "starvation" of the tissues of oxygen, from a diminution in circulatory volume In order to avert or deter such a catastrophe, certain *compensatory mechanisms* come into play, their main object being to maintain an adequate supply of oxygen to the tissues, especially to the vital organs of the body

The *minute volume* or *cardiac output* of the heart is maintained as far as possible Since $(\text{minute volume}) = (\text{stroke volume}) \times (\text{heart rate})$, the cardiac output can be maintained either by acceleration of the heart (tachycardia) or by an increase in stroke volume (from hypertrophy of heart muscle), and this is just what occurs Even dilatation of the heart has been regarded as a compensatory phenomenon by some authors

Peripheral *vaso-constriction* comes into play in order to deviate the flow of blood into the vital organs of the body

Better use is made of the blood that flows through the vital organs, this is usually effected through a slowing of the circulation, which allows more time for the dissociation of oxyhaemoglobin

When this compensatory mechanisms fail to remedy the circulatory defect, the heart becomes over-taxed and symptoms and signs of "failure" make their appearance. The picture shifts from that of *compensation* to that of *decompensation* of the heart.

Circulation may become affected in a variety of ways. Harrison, who has made an exhaustive study of the various disorders of circulation, classifies these disorders into three main groups —

Hyperkinetic syndromes, where the circulation is over-active, e.g., in hyperthyroidism, neuro-circulatory asthenia and anaemia.

Hypokinetic syndromes with inadequate circulation to the tissues. This group includes failure of the peripheral type and also acute forms of cardiac failure.

Dyskinetic syndromes, where the action of the heart becomes deficient. This group represents the chronic forms of heart failure.

The terms "circulatory failure" and "disorders of the circulation" are not synonymous, since the latter term includes the hyperkinetic syndromes or states of overactive circulation, which cannot possibly be regarded as states of circulatory failure. Whether Harrison and his school are justified in including peripheral failure and the acute forms of cardiac failure under the same designation (*viz* hypokinetic syndromes) is open to question.

Since circulatory failure or failure of the circulation can be cardiac or extra-cardiac in origin depending on whether the heart or the peripheral circulation gives way first, it is convenient to recognize two main forms of failure.

(1) Cardiac failure, heart failure or central failure.

(2) Peripheral failure, extra-cardiac circulatory failure, or capillary failure. The word "shock" is often used to refer to this type of failure.

Peripheral circulatory failure. The medical profession is becoming increasingly familiar with this form of failure. The essential feature of peripheral failure is *loss of tone* of the peripheral blood-vessels resulting in stagnation or "pooling" of blood into the periphery and what is perhaps more important, a diminution in the venous return to the heart.

Death from circulatory failure in cases of pneumonia, typhoid and other fevers is frequently attributed by the laity and even by the medical profession to failure of the heart, as a matter of fact, circulatory failure in such cases is much more often peripheral than cardiac in origin.

Common causes of peripheral failure are —

After severe injuries, operative procedures and loss of blood from the body the well-known condition of *surgical shock* may occur. What is not realised is that a similar state of shock may arise, even more frequently, under medical conditions (*medical shock* of Aitchley).

In acute infections or infectious fevers like pneumonia, typhoid and diphtheria, there are many problems about the peripheral failure of acute infections that remain unsolved. Why, for instance, is the response to treatment so different in different cases, in spite of these cases being clinically closely similar? It is by no means unusual to

meet with typical and apparently mild cases of peripheral failure that fail to respond to classical therapeutic procedures, like the administration of fluids and sympathicomimetic drugs. It has been suggested that the aetiological factors concerned in such refractory cases may be different. It has been suggested that some of these cases may owe their origin to low blood-sugar levels (or to glucose starvation), blood-sugar estimation in such cases may reveal hypoglycaemic levels and response to glucose therapy may be gratifying. Vitamin-B deficiency has been suggested as another possible aetiological factor in some of these refractory cases, complete recovery has been described in cases of this type after three or four injections of vitamin B₁ 30mg. The refractoriness of some cases of this type to the pholedrine group of drugs has been observed. A man with pneumonia and typical signs of peripheral failure failed to respond to all the classical remedies, half a c.c. of adrenaline given three-hourly and infusions of saline had no effect, as a last resort, 5 c.c. of nikethamide was given intravenously and proved quite effective. It is possible that a cardiac failure had supervened on to the peripheral failure and a strong stimulus to the heart was necessary to set the circulation going again. Such a case is definitely exceptional, in the great majority of cases of peripheral failure cardiac stimulants of the nature of nikethamide and leptazol are better withheld, and if used, not before an adequate trial has been given to peripheral stimulants like adrenaline and pholedrine. The action of nikethamide-like drugs on the heart in cases of peripheral failure can be compared to the "flogging of a tired horse", if the primary circulatory derangement of peripheral failure, viz, a diminished venous return to the heart is corrected, then the heart will automatically resume its normal duties without any extra efforts at stimulation.

Intractable vomiting or diarrhoea, e.g., cholera. Excessive loss of fluid from the body results in a diminished blood volume which in turn leads to a diminished venous return to the heart.

After coronary thrombosis and pulmonary embolism. These conditions usually include a mixed form of failure, the heart and peripheral circulation both contributing to the failure.

In diabetic coma

During the crisis of Addison's disease

After severe burns and scalds

After perforation or rupture of intra-abdominal organs

Clinical Picture The main clinical features of peripheral failure may be enumerated —

The appearance of the patient is often characteristic, he is either deathly pale with a "cadaveric hue" or displays a "greyish cyanosis", quite unlike that of cardiac failure. A blotchy condition of the skin (cutis marmorata) is evidenced in severe cases. The state of consciousness may vary considerably, he may be drowsy and apathetic or fully conscious and restless.

The extremities (and sometimes the whole body) are cold and clammy, in spite of low skin temperatures, the rectal temperature is usually high.

The pulse is characteristically weak and sometimes "thready", a

low tension pulse is almost constant in these cases. The rate of the pulse is raised and may be 140 per minute or more. The severity of a case is not necessarily proportional to the rate of the pulse, the latter being dependent on a variety of factors. Fatal forms of peripheral failure may arise in cases of typhoid, peritonitis and in pneumonia with meningism, with pulse rates of not more than 100 or 110.

There is a sharp drop in blood pressure, the systolic pressure may fall to 60 or 70 mm Hg or less. I find this fall of pressure to be a better guide to the gravity of a case than the rate of the pulse. There is a proportional fall in the diastolic pressure. In some cases of peripheral failure it is impossible to estimate the blood pressure, either by the auscultatory or the palpatory method.

The superficial veins are frequently collapsed. There may be great difficulty in finding an antecubital vein for intravenous administration of fluids. There is usually a sharp fall in the venous pressure, figures as low as 2 cms of water may be registered. In three cases of pneumonia with peripheral failure, recently observed by me, the venous pressures, which were determined with the BD Venous pressure apparatus designed by Lester Cohen, were 3.5, 5 and 4 cms of water, respectively.

There is a diminution in the urinary output (oliguria), complete anuria, when encountered, usually means death. However, cases do occur where the kidneys start functioning again even after several days of complete suppression.

Treatment The treatment of peripheral failure falls under three heads.

Administration of fluids In order to restore the blood volume to normal and rectify biochemical alterations that have arisen in the blood. Besides transfusion of blood, many different fluids have been tried in an attempt at restoring the blood volume, e.g., normal saline, solution of gum acacia, glucose and alkalies. There are cases of peripheral failure where indiscriminate pushing in of fluids into the circulation may precipitate, rather than avert, a fatal issue. I have, on two occasions witnessed death from pulmonary oedema in cases of peripheral failure where fluids had been indiscriminately pushed into the circulation, a case of pneumonia with peripheral failure received three pints of normal saline intravenously at the hands of a house-physician, in London, within three-quarters of an hour, two hours later the patient had succumbed to acute pulmonary oedema. As a rule, it is unwise to give more than a pint of fluid at a time intravenously, if, however, sufficient intervals of time are allowed between successive pints of fluid, several pints can be introduced into the circulation daily, with safety. Some workers advocate continuous administration of fluids by a slow "drip method."

It is a point of some importance to know whether fluids introduced subcutaneously or intramuscularly in cases of peripheral failure are absorbed from the tissues. Absorption of fluids from the tissues in such cases appears to depend upon the degree of failure present, if the failure is mild or moderate in severity, absorption of fluids from the tissues does occur. This conclusion I arrived at

recently after several experiments. Cases of diabetic coma with peripheral failure have repeatedly been restored to normal by large doses of insulin, administered hypodermically only, unless we accept an absorption of fluids from the tissues in such cases, how else can we explain the response to insulin? There are, however, exceptions to this rule. In the very severe cases of "shock" with exceedingly sluggish circulation, absorption of fluid from the tissues does appear inadequate or absent. To cite a case in point. A man in diabetic coma was given 100 units of insulin, hypodermically, twice within an hour by his doctor, when seen two hours later, the patient was in deep coma with sluggish jerks and typical signs of peripheral circulatory failure. 50 units of insulin were given intravenously in a pint of saline, an improvement was noted in the clinical state within a short time. Large doses of insulin had proved ineffective in this case when given by the subcutaneous route probably from lack of absorption. Since it is difficult in practice to assess the degree of peripheral failure in a given case, no accurate and easy method being available for its determination, it is always a wise precaution to administer fluids and therapeutic remedies like insulin, by the intravenous route from the first. The arterial and venous pressures give us a rough indication of the degree of peripheral failure. With a systolic pressure over 90 mm Hg and a venous pressure of over 4 cms of water, we feel justified in administering fluids by the hypodermic route in addition to intravenous infusions.

The use of sodium lactate solution has been urged of late by Hartmann as it serves the dual role of alkali and glucose.

Vasoconstrictor drugs. Various sympatheticomimetic drugs, e.g., adrenaline, pituitrine, and ephedrine, have been used with success in the treatment of peripheral failure. They act by bringing tone to the "atonic" peripheral circulation. A drug, highly effective in this way, is Veritol (Knoll), or Pholedrine B P. Recent papers stress the usefulness of this drug in states of surgical shock.

Maintenance of body temperature. Every effort should be made to prevent the temperature of the body and limbs from falling excessively. Care should be taken not to induce burns or scalds in a "shocked patient" by the indiscriminate use of hot water bottles.

(To be continued)

RADIATION THERAPY OF NON-MALIGNANT DISEASES

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Almost every known disease has been treated by radiation and the number of conditions in which it is supposed to be efficacious is astonishingly large. It is now possible to evaluate the utility of this measure only because of the careful observations of several workers in the last few years. As a result of the sum total of this experience many conditions are found truly amenable to Radiotherapy. It is the object of this paper to review the commoner conditions met with in Hospital work.

At the K.E.M. Hospital 1252 patients were treated by radiation therapy since the year 1938. The number is reduced on account of complete stoppage of all work for 2 years due to lack of apparatus.

CASES TREATED DURING 1938-1945 PERIOD

Lesions	1938	1939	1940	1941	1944	1945	Total
Neoplasms (Malignant)	101	126	113	15	33	50	457
Adenitis Tb	76	37	74	10	93	107	403
Arthropathy	4	2	4	1	41	58	110
Keloids	22	18	13	2	16	22	93
Skin	2	0	4	—	—	7	13
Lymphogranuloma	3	4	2	1	—	2	12
Rhinoscleroma	3	3	11	2	2	3	24
Thyrototoxicosis	1	—	2	—	—	2	5
Menorrhagia	5	15	15	8	5	4	47
Edometriosis	1	—	—	—	—	—	1
Mastitis	6	4	—	—	—	—	10
Sterility Amenorrhoea	—	—	14	8	7	5	34
Malarial Spleen	—	—	2	—	—	—	2
Leukemias	3	3	7	2	1	3	19
							1235
Miscellaneous							17
Total							1252

A glance at the figures reveals that although the number of malignant disease is large there is a steady increase in the number of patients treated for inflammatory conditions, Arthropathies and Endocrine disorders. This is in keeping with the wider appreciation of the beneficial effects of Radiation treatment everywhere. X-ray therapy is no longer limited to the field of Cancer and allied conditions. It is unnecessary to discuss benign neoplastic conditions for which it is so commonly used as for example in Hemangioma, Benign Giant cell Tumours, Fibro-myomata and Pituitary tumors. Consideration of its use in skin diseases of various kinds is also superfluous.

The treatment of inflammations acute as well as chronic has received great impetus during the last few years. Freund had reported successful results many years ago but it was for Desjardins to establish its importance and attempt an explanation of the prompt results obtained. A number of acute inflammations like furuncle,

A lecture delivered at the 57th Meeting of the G. S. Medical College and K. E. M. Hospital Staff Society held on March 9, 1946 with Dr. Z. J. Joseph in the chair.

carbuncle, erysepelas, cellulitis, gas gangrene, acute parotitis, pharyngitis, tonsillitis, lung abscess and even virus pneumonia have been successfully treated by workers too numerous to mention, individually. Subsidence of pain and swelling and quick resolution are observed. If suppuration is already set in it is hastened. The clinical observations are amply corroborated by experimental proof. Finzi and Freund studied the effects of radiation on an incisional wound and found that the part treated heals more quickly than the untreated. The resulting scar is also smoother. Borak studied numerous serial sections of treated Furuncles and obtained histologic proof of quicker resolution and quicker absorption of debris.

Kelly and Cooper and lately Cantrill have proved the efficacy of Deep X-ray therapy in Gas gangrene. Good results were obtained whether Serum was given or not.

With the advent of Penicillin most of these conditions have become amenable to treatment. When and where this therapy is not available or when it fails to achieve the desired end, radiation therapy ought to be resorted to. Finzi, Pfahler, Goldman and Rai have reported in detail their experience in the treatment of inflammation which is well worth studying.

The most important group of cases of chronic inflammations as can be seen from the table is that of tubercular adenitis. It accounts for one-third the total number of cases treated here. The majority of cases thus treated showed improvement and several, complete cure. Exact analysis of figures is not available because of the difficulty of following these cases regularly. Rosh and Quinn who followed their cases from 4 to 11 years report complete regression in about 60 per cent of their cases and improvement in 30 per cent of them. Only 10 per cent failed to improve. Hauser has also made careful observations on a large number of cases. X-rays are no specific for tubercular disease. They have no effect on the *Tb Bacillus* directly. Radiation only helps to tip the balance in favour of the body and against the organism by provoking a smarter reaction and increased fibrosis in the affected part. Active destruction of the epitheloid and giant cells with increased fibrous tissue formation have been observed in histological studies of treated glands. It follows therefore that proper nourishment and proper environment are as essential for success as in any other form of therapy now available. In the absence of these failure is not uncommon. The type of patients treated in the hospital are long neglected, ill-nourished and many of them advanced cases with incipient pulm or abdominal tuberculosis. They are not the best material to assess results from.

The type of cases best suited are those with discrete small nodes located in one area. Those with large nodular masses respond slowly and with certainty. Cases with large matted nodes with early caseation improve with difficulty and the last type with fixed matted nodes and draining sinuses do poorly. For the second group viz those with large hard masses Windyer's method is worth following in hospital practice. Removal of the mass as far as possible followed by radiation therapy cuts short the time required for radiation-therapy alone and gives radiation a better chance to act on

the diseased tissue It is commonly believed that caseating nodes should not be treated by radiation Hauser has proved that with small doses cautiously given and by aspiration as often as necessary in between, good improvement can be obtained A prolonged course of ultra-violet therapy does them only a limited amount of good and many of them pass on to the stage of breakdown, sinus formation and skin-involvement

Radiation therapy seldom flares up the disease Only when supra-clavicular and mediastinal glands are involved there is a possibility of pulmonary spread Most of the time this is due to too vigorous a treatment The type of nodes whether caseating, fibrous or hyper-plastic and the general condition of the patients have to be taken into consideration in determining the dose, frequency and repetition of the treatment Dosage cannot and ought not to be uniform in all cases

Tubercular lesions of the skin such as lupus vulgaris and hypertrophic verrucous lesions respond well, tubercular peritonitis is reported by McIntosh to yield good results Tuberculosis of the adnexa has been treated by several people but its occurrence in young women of parous age makes its appliance difficult in this country Chronic simple adenitis and tracheo-bronchial adenitis following whooping cough give uniformly good results No cases of this type were treated in this series

Radiation therapy has a very important place in the treatment of actinomycosis especially of the facio-cervical type In thoracic and abdominal types it has less effect In a discussion of the value of radiotherapy on mycotic infections at the Royal Society of Medicine John Blewett reported complete cure in 25 to 29 cases of cervico-facial type of actinomycosis Williams at the same discussion presented his results with 23 cures out of 26 of his cases One patient treated by us for extensive facial actinomycosis is free from disease for the last 2 years

Rhinoscleroma, by no means an uncommon condition met with in our clinics, has been extensively treated by radiation therapy The granuomatous type responds much better than the fibrous one A remarkable case with extensive involvement of the lip, nose, nasopharynx, palate and tonsils showed almost complete regression in 6 months time Several others followed for varying periods have shown good regression Recurrences can be treated again if necessary

The latest development in this branch of therapy is the treatment of painful conditions like sciatica, lumbago, spondylitis and various types of arthritis as well as post-traumatic painful arthropathies Smyth and Freyberg have reported on a group of 100 cases They found marked improvement in 30 per cent of cases Baker studied many cases of spondylitis and found improvement in 75 per cent of cases All the cases treated by us showed alleviation of pain and stiffness Spondylitis ankylopoitica always responds while the osteo-arthritic type varies in its response Dramatic improvement may be obtained in some cases while other show little improvement Horwitz and Dillman have shown experimentally that large amount

of radiation does not injure the cartilage or synovia of the joint. No harm can be done by small amounts of radiation used in the treatment of these cases. Cases of rheumatoid arthritis may show good regression with decrease in pain and swelling although the ultimate prognosis is not affected.

Keloid treatment has received a new impetus in the recent war. Levitt and Sir Harold Gilles have firmly established by experimental and clinical proof the value of x-ray therapy. Hunter treated 491 cases and found 65 per cent cured. Hyper-plastic scars and keloids which are young, soft and pinkish, respond invariably. Old, hard and white avascular keloids and large fibromatous keloids do not give good results. As Gilles has suggested resection of an old keloid and prophylactic treatment of the excision scar by radiation is the only way of tackling the latter type. Persons with keloidal tendency develop more keloids, in spite of radiation therapy. Careful selection of cases has to be made before undertaking excision. Ordinarily treatment of the scar in about 2 weeks time prevents keloid formation. Immediate treatment in our experience tends to delay the healing of the wound and does not show the same effect as when the treatment is given after two weeks. Pre-operative treatment does not particularly help the prevention of keloid formation.

Plantar warts can be easily eradicated by X-ray therapy as well as by radium therapy. Franseen reported a large number of cases treated during a period of 16 years. He found excellent results in the majority of cases. Montgomery reports 90 per cent of cures in a series of 487 cases.

Deep X-ray therapy was hitherto regarded as a tried and trusted method of treatment in thyrotoxicosis. Stone in a recent communication reports the reduction of B.M.R. from an average of +35 to -2 per cent. Pfahler's work in this connection is memorable. The advent of Thiourasil may however replace this method entirely.

We had no opportunity of trying the use of radiation in other conditions such as trachoma and spring catarrh. It is not possible to evaluate the numerous claims made regarding asthma, Raynaud's disease, angina or hypertension for the same reason. Practical considerations compel us to limit our field to the common condition where radiation therapy has approved and a definite value.

Varying types of techniques have been followed during these years. The general principles of treatment however remain the same. For acute conditions small doses repeated at short intervals have been always used. The voltage has been near 100 to 140 Kv for comparatively superficial lesions and from 150 to 180 for deeper lesions. For chronic inflammations treatment has been given more slowly with larger individual dosage and longer intervals. Arthropathies and neuralgic conditions have received treatments at 4 to 7 days intervals. One course has generally consisted of 4 to 6 treatments to the affected area.

For tubercular adenitis small doses repeated at weekly or fortnightly intervals have given satisfactory results without any skin change except tanning in a sensitive patient. Rhino-scleroma

actinomycosis come under the category of chronic inflammations and are treated on the same general principles. For thyro-toxicosis the general conditions, B.M.R. and pulse rate are taken into consideration and the individual dose and length of the course determined specifically for each case. For keloids one large single dose, if the condition is localised and fractionated dosage if the lesion is wide-spread, have generally sufficed. In a few cases a second large dose was required to completely soften the keloid. The technical factors which mainly depend on the type of apparatus and the number of r units actually administered can be of little interest to clinicians and as such are omitted here from consideration.

FINZI AND FREUND
ROSH AND QUINN
HORVITZ AND DILLMAN
CANTRILL
JOHN BLEWETT
I. WILLIAMS
LEVITT AND SIR H. GILLES
DESJARDIN
SMYTH AND FREYBERG

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DISCUSSION

Dr M. J. Shah inquired as to the usefulness of small doses of deep X rays in stimulating bone marrow in cases of Aplastic anaemia, sulphur resistant pneumonias, virus pneumonias and gas gangrene.

Dr K. A. J. Laikka inquired whether X ray radiations would help in early cases of Leucoderma.

Dr S. G. Joshi wanted to know whether in the fibrous type of Rhinoscleroma Surgery was to be resorted to before the X ray therapy to re-establish the passage. What was the incidence of recurrences after X ray therapy?

Dr C. B. Dhurandhar inquired as to the number of cases of Spring Catarrh and Trachoma treated with deep X rays, and the way in which the eye was protected from the action of these rays.

Dr Z. J. Joseph said: 'In tubercular adenitis when there is no suppuration nor caseation Deep X ray is the best. Radiation may be given once a week in a dosage of about 60 r units. When there is the least suspicion of caseation or softening Deep X ray should be given with great caution. There is the fear of intense local reaction in the gland with marked swelling of the surrounding tissues with increase in the suppuration process. Ultraviolet Rays have a definite place in the treatment of tubercular adenitis when there is caseation. I have found that a course of ultraviolet rays very often hardens these glands and after an interval deep-X rays would be found beneficial. In tubercular adenitis of the abdominal glands it is best to treat with ultraviolet rays as it is very difficult to be certain about caseation in these enlarged glands. In prevention of keloids, preoperative and post-operative irradiation is found to be the best. X ray exposures also benefit well marked Keloids which are very large and extensive and where excision is out of question.'

Dr J. C. Patel inquired as to the reason why injections of calciferol (Vitamin D) could not replace irradiation of tuberculous glands and abdomen by U. V. Rays.

Dr J. K. Mehta wanted to know whether a localized lesion in one lung could be treated by deep X rays.

Dr S. C. Desai speaking on tuberculosis of the skin said that most of the manifestations were not amenable to radiation therapy except where the process was secondary to deep seated infection and that too in controlling the secondary infection of the skin. He further added that Madura Mycosis treated with a combination of iodides and X rays yielded good results.

Dr L. H. Athle in reply said: 'I do not believe that X ray therapy has any place in the treatment of Aplastic anaemia. There is no stimulating action on the bone marrow. Unresolved Pneumonia and Virus Pneumonia have been successfully treated with radiation. It is obviously difficult to assess the definite value of this measure. Gas gangrene as I have said earlier is definitely treatable by X ray therapy. Our experience is however limited to a few advanced cases.'

In leucoderma radiation tends to cause increased pigmentation in the hyper pigmented margins and leaves the white area along thus accentuating the defect. Leucodermic areas of skin over lying malignant growth have been intensively treated without producing any appreciable change in the lack of pigment.

When fibrous type of Rhinoscleroma blocks the nares operation may be necessary to open the passage as the radiation does not help to do this. On the other hand further fibrosis may take place as a result of healing. In the exophytic type of lesion on the other hand it is not necessary to resort to surgery. The nodular masses disappear rapidly. Recurrences are not uncommon after radiation. These can be re-treated when and if necessary.

Our experience with Spring Catarrh and trachoma is limited to a few cases. The response was quite encouraging. No harmful effects can follow if the Cornea is properly protected by a thin shield of lead adapted to the eye and inserted below the lids before each exposure. Contact therapy unit or Radium applicators are very useful for the treatment of eye conditions.

In pulmonary tuberculosis radiation has little value. It is important to remember that it can not be treated except by very small exposures for fear of flaring up the lesion. Even in case of cancer of the Lung associated with pulmonary tuberculosis is a contraindication to treatment if the focus has to be included in the field.

Tuberculosis of the skin secondary to underlying nodes as well as Lupus and Verrucous types do extremely well under X ray therapy.

The beneficial effects of U. V. radiation in the adenitis were not only due to the production of Vit. D. In what way exactly does this treatment differ from administration of Vit. D is for Radiation biologists to answer. Deep therapy does not depend on any such action but affects the enlarged glands directly.

“WHAT SHALL WE DO?”

V R KHANOLKAR

Then the bowsprit got mixed with the rudder sometimes
A thing, as the Bellman remarked,
That frequently happens in tropical climes'

Lewis Carroll:—The Hunting of the Snark

I am glad to have this opportunity of inaugurating the 8th Maharashtra and Karnatak Medical Conference. I take pride and interest in the success of these conferences. The medical men in a big province like ours are separated by long distances from their colleagues. These conferences bring them together. The doctors from big towns get to know the problems of isolated practitioners and the doctors in small places get drawn into the stream of recent medical progress. As you will soon see our colleagues in this famous city have made a great effort to make our stay with them both pleasant and instructive, and it is up to all of us to give to this conference the best that is in us of good will and good feeling.

I do not believe in making speeches for their histrionic effects. I would refrain from discoursing on the vast field of socio-political problems which have been with us for so many years and which no amount of ineffective talk is going to solve. We all know that our country is on the threshold of big decisions and that these decisions are sure to affect the future of our profession and possibly the health and happiness of our people. Let us hope that the decisions will be wisely taken and that a new era of a youthful and vigorous culture will blossom on our own soil, in our own lifetime. I do not believe in harping on the failures of others, and the shortcomings of those who have been here before us. The question is not what others have done or left undone, it is, what are we going to do, with our work, about our education and for our people. Just take one example. An All India Committee has worked for nearly 3 years under the chairmanship of Sir Joseph Bhore and has tried to survey our health problems and has offered recommendations for future developments. I have read their four volume report carefully and I must confess that it is a document embodying the sincere effort of many men who were actuated by a keen desire to get things done. Now you will find all sorts of men—and I blush to think that many of them are leaders of our profession—ridiculing and criticising adversely the whole effort, without having even taken the trouble of reading through the report. Let me state that I was not a member of the Committee, nor do I hold any brief for the report, all that I wish to state is that a lot of very useful information has been made available to us, and also to the people who will direct the future health development of our country. It is upto them to give careful thought to the various recommendations contained in the report before being led into nebulous and unproductive schemes based on emotion and dream thinking.

Being the inaugural address delivered at the 8th Maharashtra and Karnatak Medical Conference
Bijapur 1946

Other people have shown what concerted effort, led with intelligence, directive and good will can do for the health of the people. A recent example is worth our notice. Not very far from the north-west corner of our country is a small Asiatic republic 64,000 sq miles in area, with just over 6 million inhabitants. For centuries the population were a prey to invaders, robbers and exploiters. The peasants were pitifully poor and lamentably ignorant. Only 2 per cent of the population could read and these were mainly the Mullahs. The women lived in mediaeval servitude and were stoned in public squares if they discarded the veil. Those of you who are acquainted with Persian poetry must have had romantic visions of Samarkand and Bokhara from the beautiful verses of Shaikh Saadi and Hafiz. The romance and quaintness was a flimsy cloak, barely concealing the canker beneath the surface. The extreme poverty of the people, the devastating prevalence of infectious diseases, the totally insanitary living conditions could well have reminded us of some of our very backward areas. But that was twenty-five years ago. Two decades of planned effort by the Government, and co-operation by the people has converted this land of festering disease into one of the most progressive and 'prosperous republics in Asia. Just look at the condition of health services

	Hospital beds per 100 pop	Doctors
U S A.	4 810	1/760
U K	7 14	1/1000
Turkmen S.S.R	4 60	1/2807
Uzbek S S R	3 8	1/2876
Rhodesia		1/68 000
Gold Coast	0 33	1/68,200
British India	0 24	1/6 800

Turkmen S S R (1937)

Number of maternity and infant welfare centres	62
Number of maternity beds in hospitals	325*
Number of places in permanent creches	6 239
Number of kindergartens and nurseries	480
Number of playgrounds	1,881

* Or 1 for every 3,858 of population. The corresponding figure for Britain is 1 for every 4,500 of population approx.

Can we take a leaf out of the book of these people and try the methods which have been eminently successful with them? I believe we can, at least in two respects. First, we should train many more doctors, pharmacists, nurses quickly and at the same time create a keen desire in our people for cleaner living and better health. How did these people strive to achieve this two-fold aim? I believe that their greatest contribution in this direction was the evolution of a concept of "positive health". This concept implied the simultaneous and conjoint action by the medical authorities of the state and also by its every individual component. They considered that it was not only desirable to improve the health of the people, but that it was the duty of every citizen of the republic to remain healthy and combat disease-promoting conditions. It was incumbent on the state to provide facilities for this purpose, but it was also obligatory on every citizen to assist the state in the total utilisation of all such

facilities This concept was the opposite of a few weary, disillusioned officials forcing health measures on an unco-operative and unsympathetic population As you are aware there is a wide divergence of opinion regarding educational methods People in Turkmen SSR have approached them by training their people in their own language Twenty-five years ago there were 8,000 Hakims without any pretension to a knowledge of modern medicine in the Bokhara Khanate There was only one doctor who attended the Emir, his harem and his court They attempted to control Malaria, which was a terrible scourge in the country, by paper pills with holy or mystic inscriptions In 1937 there were 481 doctors All children attended schools and there were 25,000 students in higher educational institutions being trained as agronomists, engineers, doctors and teachers The upsurge in the cultural advancement of the people followed an equally phenomenal progress in the language of the region Books, journals and newspapers were published to meet this ever increasing demand. When we compare this roaring river of progress with the thin trickle of our own advance we are not surprised that people still discuss and orate on the unsuitability of our languages for scientific education I hope you will permit me to digress for a moment into this question of language as a vehicle of human progress

Man probably made the most momentous stride in his intellectual development when he began to name the objects with which he came in contact in his daily life He created an instrument which enabled him to peer through the sense barrier of time and space which was closely hemming him in An animal has no cognition of time, before or after the span of his own life, nor beyond the local portion of space in which his body moves about Man has been able to visualise great stretches of space and to speculate about the happenings in widely separated periods of time by creating a system of symbols which we call language The other day Prof Athavle was able to narrow down for us the date of one of the happenings of Kuru War to 28th October 3016 B.C., and to give us a vivid description of the happenings from Ur to Hastinapur round about that time The use of language however, has been a double edged weapon in our feeble hands Very early we began to confuse the word or the symbol with the object which was meant to be symbolised We began to bestow attributes to the word which it could never possess We imposed the devious pattern of our own words on the natural order of things All this has resulted in confusion, superstition and misery for human beings Take the case of medical education We in this country strive to learn books and not subjects We fail to distinguish, that which has been woven by our imagination, from that which exists in the outside world The idea of verifying verbal explanations and understanding scientific medicine is lost in a babble of canned phrases The words go round and round in our head, as a convenient currency for passing examinations or pacifying patients, without conveying any productive information It is evident that we could never contribute to scientific medicine unless the meaning of what we read and hear is correlated with what we perceive with our senses and deduce with our reasoning faculty I believe that this would

be only possible when we start learning medicine in our own languages rather than just memorising foreign texts

The next consideration is that there should be an altered outlook and a complete change of heart in our own profession. Our ideas regarding the measures for combating disease are an outcome of the conditions prevailing in our country and abroad some five centuries ago. In both places, the existence of a class or caste system in the people was an accepted fact. There was the highborn, the rich and the powerful and there were the poor, the unprivileged and the unfortunate. It was natural that the former should get better treatment, special consideration and specialist attention. Treatment in charitable institutions, mainly carried out by the honorary effort of doctors was "suitable for poor persons". The argument was often advanced that if the staff, equipment and remedies in these institutions were hopelessly inadequate, the charity patients neither desired nor deserved anything better. If the food was bad, the treatment uncivil, the beds uncomfortable and insanitary, the poor were accustomed to nothing better in their chawls. It is not surprising that our rich elected representatives on legislative bodies always referred to hospitals as white elephants. None of us had even stopped to think and find out why it was necessary to have palaces and chawls. Why there was abundance and waste on one hand and hunger and famine on the other. If we had reflected for a moment we would soon have realised that so far as medical profession was concerned there could only be one principle "equal treatment for equal needs". "In many fields we can fairly salve our consciences, at any rate for the time being, by applying the principle of the "national minimum" below which no one is to be allowed to fall, we can tolerate large differences above the minimum. It does not so much matter, except in times of special scarcity, if some people eat too much, or have too many clothes, provided everybody had a tolerable allowance of these things. But in the case of medicine the minimum is bound to approximate to the standard, for medical attention, save in quite exceptional cases, is not a luxury but a need". The health of the whole community and the best available treatment of a sick person is our collective responsibility from which we could neither shrink nor shirk behind safeguards, reservations and privileges.

I have ventured to state opinions, debatable opinions. I hope they will give you a few sleepless nights

(Continued from page 172)

also be bestowed by you on your teachers and that you would attain still greater success in the practise of a profession whose members you now aspire to become

The time for meaningless talk, aimless wanderings, frequent holidays and festivals is past with your adolescence. There is a job of work to be done. You have got to do it, so gird up your loins and get going

"WORK TO BE DONE"

V R KHANOLKAR

A few days ago I was asked to deliver an inaugural address to the new students of this college. It was expected that I should offer them some advice at the commencement of their career. I have readily consented to do so. Firstly because delivering lectures is a habit that grows and it is the privilege of age to be garrulous, and secondly because I am genuinely fond of the young. I find so much in them to hope, cherish and esteem. You may be surprised if I were to tell you that I keep learning more from my young colleagues than they do from me. However, I am going to deviate from the original suggestion which was made to me. I am not going to offer you any advice. It is the experience of most people that advice is rarely followed, except perhaps by those, who do not need it. I am going to tell you about the obstacles and pitfalls which beset my path as a student and which may embarrass you if you have not been forewarned.

I encountered four big stumbling blocks in my path as a medical student, and because fortune favoured me I was not deterred in my progress by any of them. The first was the medical books. You have probably been reading nice handy editions, on elements of different subjects. Now you would be faced with cumbersome volumes and hefty tomes, which will weigh heavy on your heart when you start to read them in your beds. My first reaction to them was one of dismay. I wondered how I could ever get to know all that was stuffed in those closely printed pages. I dare say you have already despaired at their size and contents. Some of you may react to their unwieldiness by keeping them unopened, and warding off the evil day for opening them until just before some examination. If you do so, you would acquire an extreme distaste for books now and for a long time to come. If however, you begin to read your books and refer to the printed word for correlating it with what you observe day by day in the laboratories and the clinics, you may be surprised how easy the whole learning becomes. Facts and figures seem to stick to your mind without effort and without fail in the course of your routine work. Gradually and insensibly you grow in knowledge and amass ideas and information as you go along. The only condition appears to be that you should do your reading and your work methodically and deliberately, without interruptions and without anxiety. That is how I managed in my student days and I still continue to wonder how it was possible to wade through so many books, reviews, journals with little systematic reading in a fairly short time. You remember the last time you went up a mountain side, along a gentle slope, with pleasant companions. When you had reached the summit you marvelled as you looked at the plains below, that you had reached an eerie height without the effort of a strenuous climb. You would be surprised how soon the reading habit grows on you, and I can promise you many pleasant moments with your books, when you have taken to liking them.

Inaugural address delivered to the students of G S Medical College Bombay on 11th June, 1946

My next obstacle was my teachers. I have come across four types. The first type of teachers are those who have an irresistible urge to teach. They must teach someone something or be utterly miserable. These are born teachers, irresistible teachers, and in their company one is caught up in the glow of their enthusiasm. Somehow the scales of ignorance fall away from one's eyes after an explanation of a seemingly difficult problem and one begins to wonder why the thing had not been so simple before. My friend Shirwalkar was a teacher of this type and this institution suffered an irreparable loss in his early demise. The second type are men of profound learning, keen intelligence and original thinking. These are the born investigators. They have added vastly to the store of our common knowledge. Unfortunately they are unable to appreciate the difficulties of us common folk, and they certainly do not suffer fools gladly. They have neither the patience nor the inclination to make difficult things easy for others. My teachers Bayliss and Sidney Martin were men of this type. But what a privilege it was, when one got to know them better in the intimacy of their laboratory or the quiet of their wards, undisturbed by jostling crowds and noisy seekers after diplomas. The third type are the rarest of all. They possess not only a neat ordered mind stocked with prodigious learning, but they are also blest with a clarity of expression and a lucidity of exposition which makes devotees of their students, and apostles of their assistants. I consider myself extremely fortunate that I came across three such remarkable men during my life as a student. The first was my chief Boycott, then there was the great surgeon and thinker Wilfred Trotter and finally the pathologist Erdheim. These teachers are the salt of the earth and you would be fortunate indeed if you had some such teachers in your time and got to know them in the intimacy of their homelife, as well as in the stir of their workplace. They are the catalysers who convert our work-a-day world into a land of wide spaces and far horizons. These three types of teachers are unfortunately far too few, and alongside of them I met far too many men of the fourth type who puzzled me a lot. They were most of them clever people, experts at some technique or another, possessed of smart manners and glib talk. But they were little men, neither teachers nor investigators, men with confused thinking, selfish, obstinate, opinionated. Men of small minds who had somehow found themselves in jobs which involved teaching of students. The impressions they have left on my mind are blurred with the passage of years and I recollect only the fads and clever sayings of some, or the little obsessions or mannerisms of others. The colour of their ties, the cut of their clothes, and the make of their cars lingers longer in my memory than the words of wisdom which fell from their lips. They appeared to be play-acting most of the time. Their main effort seemed to be directed to demonstrating how every one else except themselves, was thoroughly ignorant and how they were the only clever people about. Teachers of this type are a misguiding and bewildering stimulus to their students, and I hope you will escape being influenced by any such people.

Several years later I became a teacher myself, and I kept con-

stantly before my mind the directions given by a great teacher to his colleagues. A teacher "must not only teach. He must not only engage in original research intended to advance science. He must also endeavour to provide the young people who are emerging to scientific life, the physiologists, biologists, physicians—our students of today, our successors of tomorrow—with clear and precise directions that will enable them to avoid the hesitations, the gropings, the disappointments, the errors, the discouragement, all those miseries of the beginning of a scientific career. He must provide them with directions that will guard them against hasty generalizations, *a priori* assumptions, brilliant theories. The young people are unaware of the treachery of these brilliant theories, and with all too generous enthusiasm admit them to the inner circle of their scientific life, just as they, by the way, admit to the inner circle of their private life the brilliant companion who has seduced them by his *esprit* but who only waits for an opportunity to deceive and betray them."

The next hurdle in your way is the hurdle of examinations. I see some of you sailing over them merrily, others spending miserable months and years getting through them, and still others finding them insurmountable obstacles. I have had a long experience of examinations. Some twenty-five years of my life I have submitted myself to them, and another twenty years I have subjected others to their vagaries. I have therefore some knowledge of the way they are conducted. There are two types of examiners and you would do well not to be afraid of either kind. The first type know their subject well and also the ways of finding out what a student really knows. These men may appear distant and unsympathetic, but they are really kindhearted persons who would like to help every candidate within the limits of their instructions. They expect you to give clear candid answers to simple questions and you will rapidly acquire the art of doing so. The so-called "coaching classes" are really designed for making you experts at saying the right things to the right examiners. There is the other type of examiners—I hope you will not come across many—who do not know the job of examining and who are also innocent of the subject of examination. These people are mainly concerned with masking their ignorance and finding out what the students do not know and making the candidates feel thoroughly unhappy. There is no remedy against them, except, perhaps prayer. You should not despair if you fail at their hands, nor feel elated if they pass you. I must confess, that I am thoroughly dissatisfied with the existing system of examinations. At their best, they are a very rough index of a candidate's ability, at their worst, they are a devilish mechanism of unfairness and dishonesty. I am looking forward to the day when most examinations will be abolished and only the day-to-day progress of the student will determine his aptitude.

The main obstacle in the path of a medical student could be his own self. The distractions on his way are multiple and frequent. It is essential that he should obtain clear ideas regarding his aims

* Maurice Arthus *Philosophy of Scientific Investigation* (Preface to *De l'Anaphylaxie et de l'Immunité* 1921) Translated by Henry E Sigerist, Baltimore 1948

and the place he should occupy in the new developments which are due to be ushered in our country. The aim of a medical student is to become an efficient doctor, and finally to help in implementing a health programme which will benefit the mass of our people. Yours will be a glorious opportunity, because you will be called upon, not only to make a living by your profession, but to occupy a place, probably an important place, in a great enterprise which none of your predecessors had ever dreamt of. Your training should therefore be directed not merely towards passing certain examinations, but towards your preparation for the task which awaits your active participation. In a century of an explosive development of scientific knowledge, your approach to your studies should therefore be honest and realistic.

The first thing that I had to learn as a student was that medicine could not be taught, but that it had to be learnt by one's individual effort. My teachers could at best direct me here or guide me there, but success depended entirely on the interest I cultivated in my studies, on the way I participated in the work in the classroom, the laboratory and the clinic, and more than anything else, on the integrity of my character as a student and as a doctor. Your experience, I believe, would be no different from mine. You will notice much slackness and incompetence among your colleagues, you will see much pain and suffering in your patients. This should not allow callousness to replace the humane attitude in you, which should be the leading attribute of a good physician. You should never allow indolence or indifference to creep in on you, at any stage of your development. Do not get into the habit of putting off to-day's work to some other day, or passing it on to some other person. You would never be a credit to our profession if you do so, however brilliant and successful you may be otherwise. Let me assure you that the opportunities which are now open to you in these institutions are great and you are among the chosen few who should not betray their trust.

You will be told that yours is a noble profession, that life and death hang on your slightest movement. All this is moonshine and you will have plenty of time to discover the falsity of this and many other fables with which romantic people delude themselves and others. Our profession is like any other profession. It could be made noble if the men and women who practise it, accomplish their task with courage, fortitude and selflessness. If the work is carried out with selfishness and dishonesty it could be as mean a profession as the meanest of the lot.

Now, I look back some twenty-five years. I see before me young eager men as my students flushed with ideals and ambition. Some of them to-day are the leaders of our profession in the country. It warms the heart of a teacher to watch his students accomplish great things, better than he could have done himself. In that lies the future hope of our country. Each succeeding generation should do better than the preceding one, for the country to advance. I could only wish that the devotion and loyalty which I encountered, would

Book Reviews & Notices

MEDICAL PHYSICS Editor in Chief: Otto Glasser, with 23 associate editors Pp xlvii 1-44
with illustrations Chicago: Year Book Publishers, Inc. 1944 Price \$ 18 (Rs 81/)

An impressive book, broadly conceived and excellently published is the first impression of any laboratory worker, when it is first placed in his hands. As the different articles of one's choice are leisurely perused the admiration is enhanced by the high standard of individual contributions, the meticulous care exercised in editing, and the quality of typography, illustrations and diagrams. The editors and the publishers deserve to be congratulated on having accomplished a formidable but necessary task with exceptional ability and success.

An average medical man has very vague ideas regarding the numerous and important advances in medical physics during recent years, nor does he realise that "progress in biology and medicine have always been significantly related to advances in physics". This book is a revelation, about the important place which physics occupies today in the every day work and thought of a modern medical man.

The book consists of 23 sections each edited by a well recognised authority on the subject. The two tables of contents at the beginning and the two indexes at the end make it extremely easy to look up any particular problem, that may interest a physician. The lists of references at the end of individual articles have been chosen with great care, and include some of the very recent publications on the subject. Each article could become the basis for initiating an insight in some live topic of medical interest.

It is not possible to give a detailed review of a book which sets out to be, and actually is, an encyclopaedia, a text book and a working instrument containing pertinent data for a worker in the clinic or the laboratory.

The only drawbacks of an otherwise admirable book are its unwieldy size, and its prohibitive price, so far as readers in India are concerned. It should however find a place in the libraries of all medical institutions and the shelves of all progressive physicians and laboratory workers. There are two suggestions which may merit a consideration by the publishers for future printings. A publication in two volumes would be decidedly more handy and may be well worth the extra cost which it may entail. It is not possible to buy new copies of such books frequently and it should be seriously considered whether such books should not always be published as loose leaf editions and brought upto date every second year.

V.R K

A B C OF MEDICAL TREATMENT By E Noble Chamberlain M.D., M.Sc., F.R.C.P.
Oxford Medical Publications, Oxford University Press London 1946 Pp viii 206 Price Sh 10/6

This small book provides a brief account of the treatment of the more common medical ailments, surgical, gynaecological and dermatological and other specialized subjects being excluded.

The subject matter has been arranged in alphabetical order for ease of reference and a number of symptoms (e.g., pain, insomnia), have been included to avoid repetition in dealing with the individual diseases

The book is primarily intended for the general practitioner who wishes to make a quick reference to the essentials of treatment, and more space has therefore been devoted to the illness commonly dealt with in general practice. No attempt has been made to include measures of treatment which are not of generally accepted value. An essential feature of the book is the inclusion of diet sheets.

Most of the information given is up-to-date and the book may be warmly recommended to the general practitioners in need of a handy book for ready reference.

Reflections and Aphorisms

• • • "Great variation exists in the therapeutic philosophy of physicians. Among physicians are represented remarkable extremes, on the one hand those who utilize an almost inexhaustible therapeutic armamentarium and on the other those who use a limited number of medicinal agents in a rather conservative manner. Certainly, somewhere between such divergent opinions it should be possible to find a therapeutic philosophy that at least approaches the ideal.

For many years empiricism dominated therapeutics and during that period little progress occurred except through the random influence of trial and error. It is a regrettable fact that empiricism is still an appreciable force in present-day medicine. The overwhelming supply of so-called proprietary preparations that daily reach the physician's office through itinerant agents and through the mail would appear to make treatment of disease so easy that, perhaps, the labelling of shelves and the simple exertion of reaching for the correct bottle eventually would lead to the acquisition of a new nervous reflex. Obviously, such therapeutic efforts are not scientific and, for all their apparent simplicity, only lead the physician into a maze from which he extricates himself rarely."

• • • "The art of medicine comprises many considerations. The physician inevitably acquires a manner which on the one hand may inspire confidence, be pleasing to the patient, and at all times exhibit courteousness and sincerity of purpose, or on the other hand, by virtue of gruffness, obvious insincerity, impatience or non-committalness, may immediately create an irremediable impasse between the patient and himself. The average patient has little difficulty in appraising the sincerity of purpose of the physician which is the keynote to confidence. The physician must be dignified but it is no longer necessary to assume a painful artificial guise to accomplish dignity. There was a stage in medical history when the swallow-tailed coat, the silk hat and the bewhiskered stern face of so-called maturity were believed to be the requisites of the well-trained physicians but today no such parade enables us to hide our deficiencies.

The physician must train himself to be a practical psychologist so that he may quickly fathom the unspoken reactions of the patient which are frequently more expressive than uttered words but which may entirely escape the unwary. It is important that this appraisal be instantly accomplished, for the ensuing procedure may be dictated by a fleeting impression. The ability to delve into the psychic reactions of the patient and often to anticipate unexpressed reactions is frequently referred to as intuition. It comprises no mystic powers but only the alert interpretation of subtle expressions, both uttered and unuttered. As the physician is usually the interrogator, he should always attempt to command this advantage.

Probably one of the most difficult feats for the young medico to master, and some never learn this important lesson, is to understand that the psychologic reactions of the sick person are very likely to be disturbed, and notably is this the case with persons nervously afflicted. Thus, apparent stubbornness and what may appear to be unreasonable attitudes, and so forth, must not be countered with a forceful, adamant attitude until cautious tact and diplomacy have been exhausted."

- • "A diploma is just a license to use borrowed knowledge"
- • "If I bore you, I pardon you"
- • "No man can have a peaceful life who thinks too much about lengthening it"
- • "No man's day should ever be so long that it demands an extra drink of whisky to keep him going. No man's bank account is worth a coronary or a cerebral accident. And what fools men are to work themselves to death, paying big insurance premiums. Too often the insurance gets the widow a luxury-loving, second husband who can easily make her forget that her first husband had no time for leisure, for luxuries, for loving, or for LOAFING"
- • "What is this life, if full of care,
We have no time to stand and stare?
No time to stand beneath the boughs,
And stare as long as sheep or cows?"

Notes and News

British Penicillin now available in India We hear that Messrs Glaxo Laboratories Limited are now in a position to market Penicillin in this country. It will be recalled that although Penicillin was a British discovery, owing to the needs of war, British production has until now been earmarked exclusively for the fighting services.

Now for the first time the world's purest commercial Penicillin is available in India. It is no ordinary achievement that conversion to very large scale production has been attained within a year of the cessation of hostilities in Europe.

It may not be known to members of the profession in India that Glaxo Laboratories Limited run one of the two large scale penicillin plants in the United Kingdom, the other being a Government-owned plant at Speke in Cheshire.

House Posts—The Prince Bije Singhji Memorial General Hospitals of Bikaner have been recognised by the Royal College of Surgeons of England under conditions of paragraph 23(b) of the Regulations for the Fellowship in respect of the posts of three General House Surgeons.

Medical graduates desirous to obtain a House Surgeonship may get in touch with the Principal Medical Officer, Bikaner.

34th All India Medical Licentiates' Conference, Poona, 1946 The 34th All India Medical Licentiates' Conference will be held in Poona on 19th, 20th and 21st October 1946.

There will be a Scientific Section where papers on medical and scientific subjects will be read. There will also be a symposium on "The Problems of Nutrition in India" and members are requested to take part in the symposium as well as send their papers before the 1st October 1946 to the Scientific Committee. A medical and scientific exhibition is also being arranged.

For further information please write to the Secretaries, Reception Committee office, 502 Narayan Peth, Poona City.

Original Contributions

FAMILIAL INCIDENCE, SUBCUTANEOUS NODULE, AND LEFT RECURRENT LARYNGEAL NERVE PARALYSIS IN

RHEUMATIC HEART DISEASE

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Kutumbiah (1941), and Kutumbiah and Raman (1944) established that the rheumatic heart disease is not uncommon in the tropics and even the rare clinical manifestations of rheumatic infection are present in Vizagapatam (South India). The present paper deals with (1) Familial incidence, (2) Subcutaneous nodule, and (3) Left recurrent laryngeal nerve paralysis in rheumatic heart disease.

1 FAMILIAL INCIDENCE

Cheadle (1889) found evidence of hereditary factor in 103 of 180 cases of rheumatic infection. St Lawrence (1922) observed that in 50% of the cases, two or more members of the same family were affected. Coombs (1924) noted the familial incidence in 82 of 178 cases, and thought that the familial factor was inherent. Miller (1933) was able to get a history of acute rheumatism in parents or near relations of rheumatic children. Levine (1936) found strong familial incidence in rheumatism and considers that it is difficult to say whether it is due to a particular hereditary element or due to the same environmental conditions. He quotes an instance of two sisters and a brother who lived in different parts of England having one or more of their children affected with rheumatic infection. Poynton and Schlesinger (1937) consider that the genetic factor is more apparent in certain descendants of each generation and this with hereditary influences may be overcome by suitable environment. White (1944) found a high incidence of rheumatic infection in members of the same family as compared with those in a controlled series and he points out that three factors are mainly responsible for this familial incidence, viz, increased susceptibility, (2) close contact (3) crowded or insanitary conditions.

Symes (1905) described clear bright coloured complexion and red hair as some of the characteristics of children predisposed to rheumatic infection. Levine (loc cit) considers that pinkish colouration of the skin, freckled and red hair and hyperextensive fingers are the more important characteristics of rheumatic diathesis. Coombs (loc cit) does not agree with this view. We have not been able to find anything characteristic in Indians of Vizagapatam either in the eyes, skin or hair indicative of rheumatic diathesis.

Kutumbiah (1941) was able to find only one instance in which he could definitely trace familiar history in a series of 432 cases of rheumatic heart disease.

Familial incidence was noted by the senior author only in 4 of a series of 728 cases of rheumatic heart disease.

Family I (1943)

Father died in 1936, mother alive, not examined. (1) Eldest son, 25 years. He had low fever for some time which was suspected to be due to pulmonary tuberculosis. Examination showed enlarged heart, and systolic murmur in the mitral area. (2) Female said to have died of heart disease at the age of fourteen in 1936. (3) Female aged 15 years had rheumatic heart, mitral stenosis and regurgitation with congestive heart failure. The patient was under-developed and periods have not started as yet. Physical examination showed enlargement of the heart and presystolic murmur in the mitral area. Radiological examination showed enlarged heart, prominent pulmonary conus and straightening of the left border. Electrocardiogram showed nothing definitely abnormal except low voltage in Lead I. (4) Boy aged 14 years, had no symptoms whatsoever. He was asked to be brought for physical examination and showed enlarged heart and systolic murmur in the mitral area. Radiological examination showed enlargement of the heart more towards the right and straightening of the left border. Electrocardiogram showed nothing abnormal except flattening of T and low voltage in Lead III. (5) Male aged 11 years had stunted growth. Heart was considerably enlarged and showed not only stenosis of the mitral valve but also regurgitation of the aortic valve. B.P. 120/30. Radiological examination revealed enlargement of the heart both to the right and the left and left auricle was visualised both in the antero-posterior and right anterior oblique view with barium in oesophagus. Electrocardiogram showed negative P in Lead III and right axis deviation. (6) Male child aged 9 years had no symptoms but was asked to report for examination. His heart was enlarged and presystolic and systolic murmurs were heard in the mitral area. Radiological examination showed enlargement of the heart and enlargement of the left auricle in the right anterior oblique view with barium in oesophagus. Electrocardiogram showed negative T in Lead III and right axis deviation. (7) Male aged 7 years. This child too had no symptoms but was asked to report for examination. Heart was not enlarged but systolic murmur could be heard in the mitral area. Radiological examination did not show anything abnormal. Electrocardiogram showed low voltage in Lead I and a small Q in Lead III.

Members 3 and 5 were brought to the senior author for consultation and both the cases showed stunted growth and evidence of rheumatic heart disease clinically, radiologically and electrocardiographically. In case 3, in spite of the girl being 15 years, the periods have not yet started. All the other relations were asked to be brought for examination and 2nd, 4th, 6th and 7th members of the family showed evidence of rheumatic infection. On further questioning, information was obtained that the eldest member of the family was treated somewhere as a case of pulmonary tuberculosis. He was asked to be brought to Vizagapatam and clinical examination showed that the condition was only one of acute rheumatic fever with involvement of the heart. This is an instance in which all the members of the family were suffering from rheumatic heart disease.

Family II (1944)

(1) Father aged 36 years, (2) mother aged 28 years, (3) first boy 12 years old (rheumatic heart disease), (4) girl aged 3 years, no symptoms whatsoever. (5) Maternal uncle of the patient, aged 50 years, normal. (6) Boy, son of the maternal uncle, aged 16 years, normal. (7) Boy, son of the maternal uncle, aged 13 years, had rheumatic heart. (8) Girl, daughter of maternal uncle, aged 10 years, normal. (9) Boy, son of the maternal uncle, aged 5 years, had rheumatic heart. In this family Cases (3) and (7) were admitted as patients. Case (3) on radiological examination showed not only rheumatic heart but also Azygos lobe of the lung. All the members of the family were investigated for the Azygos lobe and Case (9) was detected by radiological appearances to have rheumatic heart. Clinical examination of this child showed enlargement of the heart and systolic murmur in the mitral area.

Family III (1945)

Father and mother alive and there was no evidence of rheumatic heart. First child died 9 days old, 2nd child died 11 months old, 3rd child died 6 months old, 4th child 10 years old had rheumatic heart, mitral stenosis and regurgitation and rheumatic nodules, 5th child, a boy 6 years old, was normal, 6th child, boy 3 years old, had dilatation of the heart and systolic murmur in the mitral area, 7th child, one year old was normal. In this family, the fourth child was admitted in August 1945 and all the members of the family were investigated for evidence of rheumatic infection and the 6th member was spotted clinically.

Family IV (1945)

Female aged 18 years was admitted with symptoms of rheumatic heart, mitral stenosis and regurgitation with congestive heart failure. She used to get occasional attacks of extra systoles. Her sister aged 30 years was admitted in the same year with polyarthritis of rheumatic origin and all the joint symptoms rapidly disappeared with salicylates.

All the seven members of the 1st family were affected and mother was the only surviving relation that was not examined. In family II, 3 out of the 9 members were affected with rheumatic infection.

in family III, 2 out of the 7 were affected, and in family IV, although all the members of the family were not available for examination, two were infected. The incidence of 4 in a series of 728 is a small percentage when compared with the high familial incidence observed by others from different parts of the world

2 SUBCUTANEOUS RHEUMATIC NODULE

Although credit has been given to different authors from 1763 onwards, the first authentic record of the occurrence of the subcutaneous nodule in rheumatic infection was that of Wells in 1810. Meynet (1875) reported the first case in France in a boy of 14 years and the condition is known as "Meynet's nodule" in the French literature. Isolated cases have been reported by different authors from different parts. Barlow and Warner (1881) published an exhaustive clinical study from 27 cases in younger individuals. Cheadle (1889) considered the presence of nodules especially on the back as a death sentence. Coombs (1924) followed up 16 patients who showed crops of subcutaneous nodules at some time or other in the course of rheumatic heart disease. Poynton (1925) found nodules in 94 cases from 1,108 cases of rheumatic heart in children under 12 years. Dieulaide (1937) observed in a series of 141 cases of rheumatic infection in China 14.9% with rheumatic nodules. Kutumbiah (1941) found only one instance of rheumatic nodule of the scalp in a series of 432 cases.

The following is a brief summary of the case admitted under the senior author —

P.P., Hindu, male child aged 10 years was admitted on 5-8-45 with a history of fever, pain in the joints and palpitation of one month's duration. The complaint started one year ago with fever and pain in the joints which used to appear and disappear at frequent intervals. The father and mother of the child are alive. The familial incidence (family III) is shown elsewhere in this paper.

Physical examination showed a poorly nourished individual. There was neither anaemia, cyanosis nor oedema. Tonsils were enlarged but not inflamed. Heart was enlarged, left border 1" external to the mid-clavicular line and right border just external to the right lateral sternal line. Mitral area showed a pre-systolic thrill. Presystolic and systolic murmurs in the mitral area, systolic murmur with accentuated 2nd sound in the pulmonary area and faint systolic murmur in the aortic area were heard. Tricuspid area was normal. Lungs showed few crepitations at the bases and liver was just palpable below the costal margin. There was no evidence of chorea.

Subcutaneous nodules were seen over the spinous processes of the 4th, 5th, 6th and 7th dorsal and 4th lumbar vertebrae (Fig 1). There was no evidence of nodules anywhere else. Radiological examination of the heart showed enlargement of the heart, prominent pulmonary conus and enlarged left auricle. B.P. 84/56. Urine was normal. Motion showed no ova, no protozoa. Blood R.B.C 4.8 millions. W.B.C 14,200. Poly 62, Lymph 28, Mon 4, Eos 6, Hb 84%. Blood smear did not show anything special. Sedimentation rate was 46 m.m. at the end of one hour (Westergren).

The patient was running a low temperature between 99 and 100°F. He was put on 45 grains of sodium salicylate per day and the fever

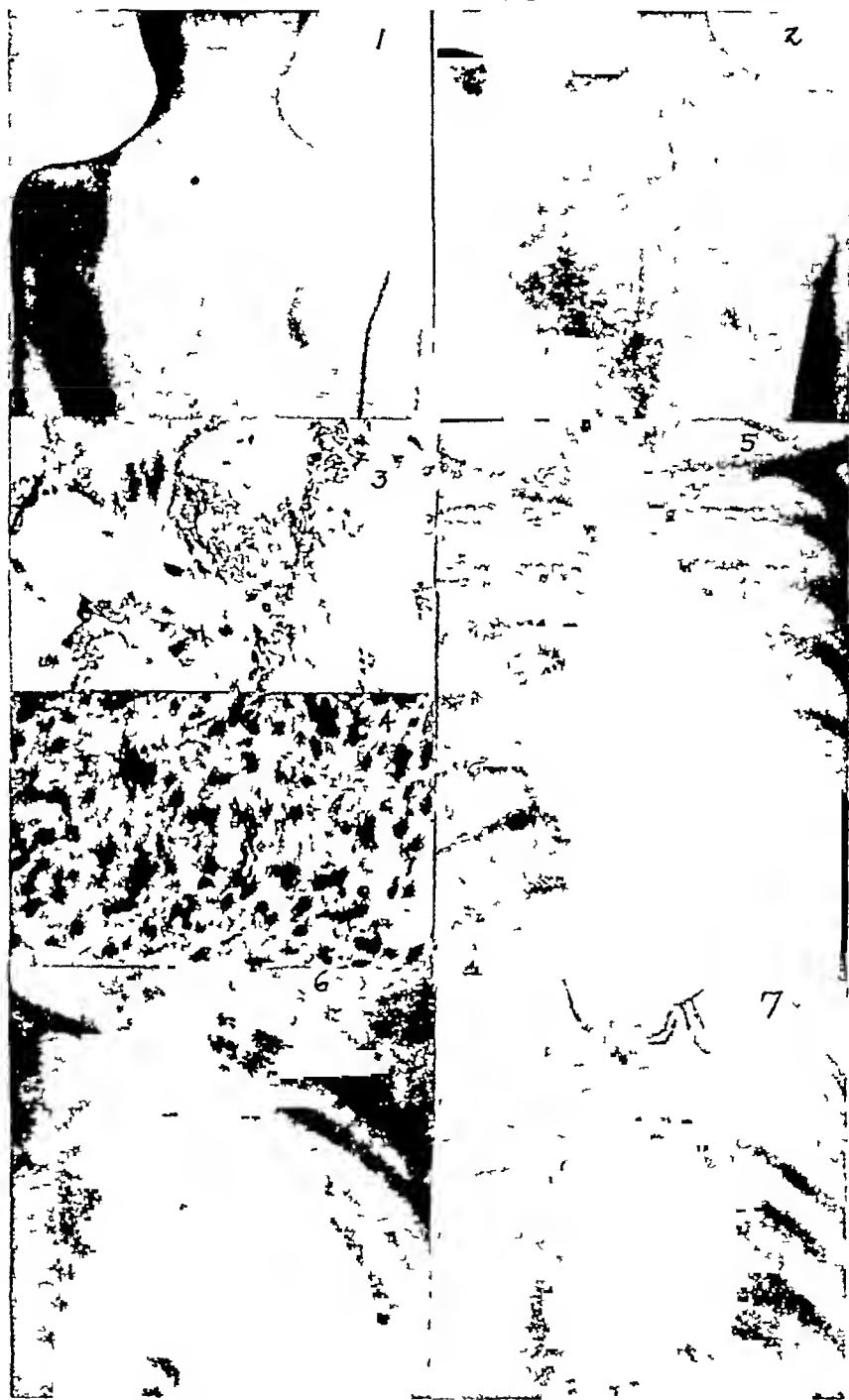


Fig 1 —Clinical photograph (taken on 2-8-45) of the rheumatic nodules over the spinous processes of the 4th, 5th, 6th and 7th dorsal and one over the 4th lumbar vertebrae (not clearly seen)

Fig 2 —Photograph (taken on 13-9-45) of the same patient showing the disappearance of the nodules and a scar of the removal of nodule over the 7th dorsal spine

Fig 3 —Micro photograph of the section of the rheumatic nodule under low power

Fig 4 —The same nodule under high power

Fig 5 —Radiogram of the heart showing the abnormally prominent pulmonary conus in the series of left recurrent laryngeal nerve paralysis

Fig 6 —Right anterior oblique view of the same case as in Fig 5 showing the abnormally prominent pulmonary conus and the enlarged left recurrent laryngeal nerve

Fig 7 —Case No. 3 in the left recurrent laryngeal nerve view with barium in oesophagus showing enlarged left recurrent laryngeal nerve

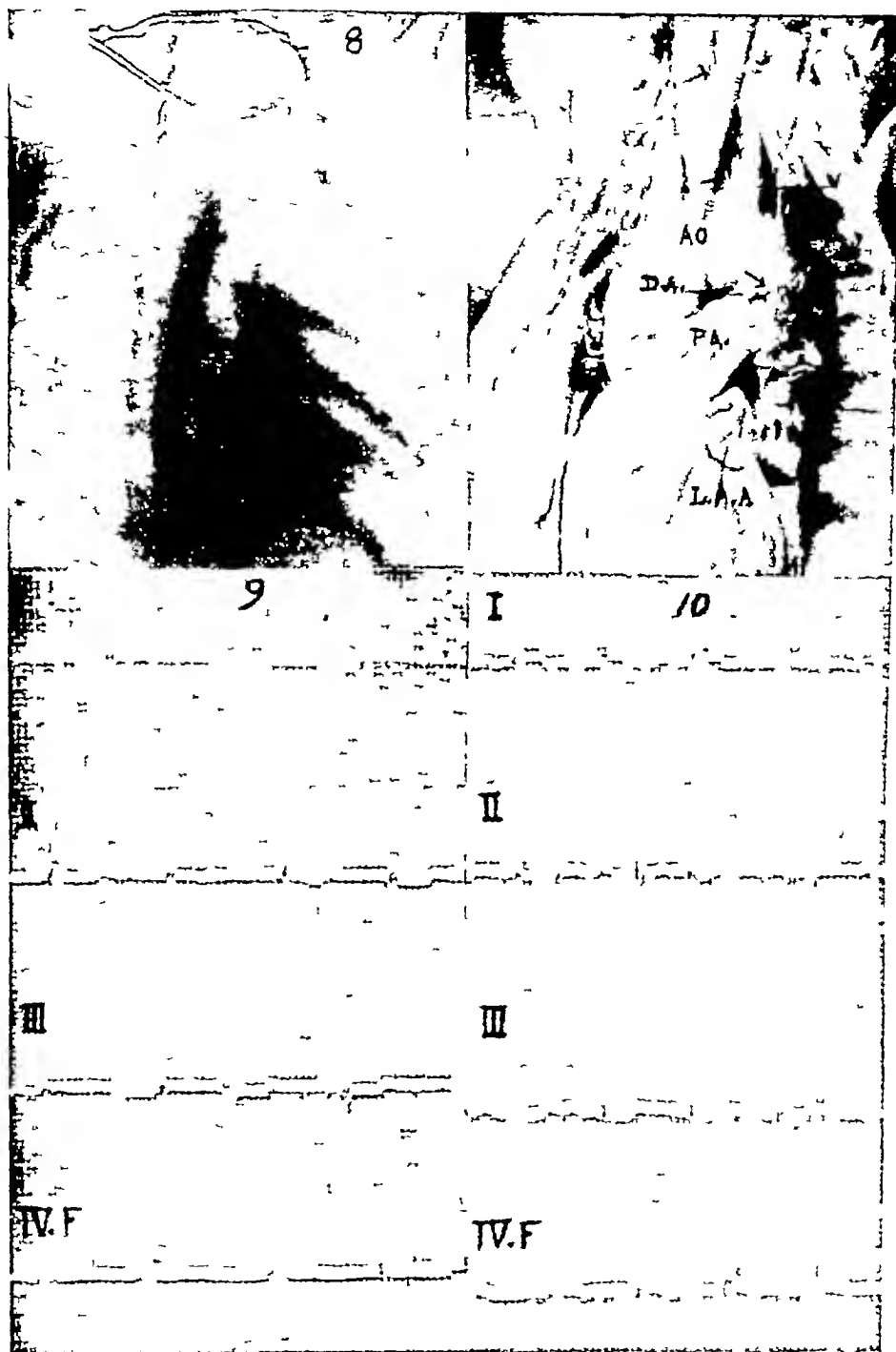


Fig 8. Same case as in Fig 7 showing reduction in the size of the left auricle after treatment of the congestive heart failure.

Fig 9. Electrocardiogram. Leads I, II, III and IV.F. (Case 3 of the left recurrent laryngeal nerve palsy) showing sinus tachycardia (120 per minute), I-R interval 0.2 of a second, I-lead deviation of S-T segment in Lead I with exactly opposite changes in Lead III and right axis deviation.

Fig 10. Electrocardiogram. Leads I, II, III and IV.F. (Case 4 of the left recurrent laryngeal nerve paralysis) showing auricular fibrillation (200 per minute) and right axis deviation.

Fig 11. Photograph of the dissected specimen showing the relationship between the left recurrent laryngeal nerve arch of the aorta, pulmonary artery and left auricle. AO, Aorta; DA, Ductus arteriosus; PA, Pulmonary artery; LAA, Left auricular appendix; V, Vagus. The three arrows represent the three different levels of the recurrent laryngeal nerve.

was controlled. A nodule was removed on 28-9-45 and microscopic section showed a segregated nodule deep in the subcutaneous tissue surrounded by fat cells. A collection of histiocytes with round and oval nuclei, a few polymorphonuclear leucocytes here and there and a few thick walled capillaries could be seen. There were no Aschoff cells (Microphotographs Figs 3 & 4 see Plate I)

The nodules became smaller and completely disappeared on 13-9-45 (Fig 2). The condition of the heart showed reduction in the size but the auscultatory findings were the same. Blood examination at the time of discharge on 22-9-45 showed R.B.C 4.1 millions, W.B.C 10,000, Poly 44, Eos 10, Lym 38, Mon 8. Sedimentation rate showed slight reduction, 36 mm per hour.

This is the 4th child of family (III) that showed familial incidence. The child was discharged on 22-9-45 with complete disappearance of the fever and the rheumatic nodules. He was seen again 4 months later when the same mitral stenosis was present without any evidence of recurrence of the rheumatic nodule.

Subcutaneous rheumatic nodules are common in England, but rare in America (White, Poynton and Schlesinger, loc cit). They occur usually in children, varying in size from the smallest palpable 2 mm to the biggest measuring 20 mm in diameter. They arise from tendons, ligaments, superficial aponeurosis and periosteum and can be palpated under the skin which is freely movable over the nodules. The frequent sites are elbows, ankles, occipital bone, wrists, spines of the vertebrae and borders of the scapulae (Findlay, 1931). They are painless and occasionally symmetrical, but in adults nodules may be found anywhere. Radiological examination does not reveal any shadow. They usually come and go, the average duration being 4 to 6 days, occasionally they are present for a few weeks, and in one case which relapsed it lasted for six months (Keil, 1936). The total number of nodules vary from a solitary one to hundreds, and as many as 200 nodules have been recorded in a single individual (Cheadle, Josias).

The term rheumatic nodule is applied only to subcutaneous nodules appearing in association with rheumatic heart or with other manifestations of rheumatic infection. Coombs thinks that the subcutaneous nodule is the most "rheumatic" of all its clinical manifestations and that the presence of the nodules indicates that the body has received a heavy dose of infection and the heart has already been damaged by that time. The presence of these nodules indicates not only the severity of the infection but shows the lesion is still active (White).

The nodules that can be seen or palpated are composed of an aggregation of sub-miliary nodules. Coombs has shown the similarity of the histological structure (viz, vascular origin, productive nature and formation of giant cells) between the subcutaneous nodule and Aschoff's nodule occurring in myocardium. The microscopic appearances have been dealt with exhaustively by Keil (1938). Three zones are described. (1) The inner necrobiotic core which consists of proliferated connective tissue cells and secondary necrosis occurring simultaneously or some time later. The degenerated areas are in-

vaded by polymorpho-nuclear leucocytes (2) The mid-cellular layer occupied by cells and basophil protoplasm with occasional large single or multi-nuclear cells having some faint resemblance to Aschoff's cells in the myocardium (3) The outer layer or the peripheral zone where there is no evidence of any capsule, vascular and oedematous elements are prominent and the number of capillaries are so many as to stimulate renal tubular structure Occasionally smaller haemorrhages can be seen

Subcutaneous nodules other than those of rheumatic origin and nodules occurring in rheumatoid arthritis in children (Still's disease), and in adults present difficulties in diagnosis The involvement of the heart with or without other clinical manifestations of rheumatic infection will be the clinching point in the diagnosis Recently, a male aged 30 years presented himself in our out-patient department with a history of polyarthritis Examination showed a small nodule in the palm of the right hand Heart was normal Biopsy of the nodule showed that it was not rheumatic in origin Saphir and Well (1923) consider the Aschoff's body in the myocardium to be of a specific tissue reaction and the subcutaneous nodule of non-specific tissue inflammation Although the pathological findings are suggestive and may be stimulated by other conditions, clinical features in association with rheumatic heart should be the main criterion for the diagnosis of subcutaneous rheumatic nodule

3 LEFT RECURRENT LARYNGEAL NERVE PARALYSIS

Ortner (1897) described the first case of paralysis of the left recurrent laryngeal nerve in mitral stenosis Fetterolf and Norris (1911) found from frozen sections that the condition is due to pressure on the recurrent laryngeal nerve by the left branch of the pulmonary artery which is lifted up by the enlarged left auricle Garland and White (1920) reviewed the literature and added nine more cases bringing the total number to seventy Coombs (1924) reported a case of mitral stenosis and chorea in a lady of 27 who was sent to him by Lacy Firth for left recurrent laryngeal nerve paralysis The condition has also been observed by Osler and Gibson (1927), Cotton (1937), White (1944) and others In a series of 728 cases of rheumatic heart disease observed by the senior author for the last twelve years (1934-1945), 4 cases of left recurrent laryngeal nerve paralysis were seen in association with mitral stenosis A brief summary of these cases are given below —

Case 1 —G V, Hindu, male aged 40 years, was admitted on 10-5-41 with a history of cough, dyspnoea and oedema of the legs of 5 months duration

Physical examination showed a fairly nourished individual with cyanosis, well marked clubbing of the fingers and signs of congestive heart failure The heart was enlarged, the left border $1\frac{1}{2}$ " to the left of the mid-clavicular line and the right border just external to the right lateral sternal line Systolic and diastolic murmurs were heard in the mitral area and accentuated 2nd sound in the pulmonary area Sounds in the aortic and tricuspid areas were normal Liver was enlarged and tender, free fluid was present in the peritoneal cavity and both lungs showed congestion of the bases Blood

pressure 100/40 Urine showed a trace of albumin and a few R.B.C but no casts

Radiological examination on 13-5-41 showed enlarged heart, prominent pulmonary conus and straightening of the left border

The patient had slight hoarseness of the voice and laryngoscopic examination showed paralysis of the left vocal cord due to pressure upon the left recurrent laryngeal nerve

The patient was treated with digitalis and diuretics by mouth and mersalyl injections and was discharged on 11-6-41 He could not be followed up further

Diagnosis Rheumatic heart, mitral stenosis with insufficiency and paralysis of left recurrent laryngeal nerve

Case 2—R.A, Hindu, male aged 30 years, was seen on 7-2-44 with symptoms of dyspnoea and palpitation of 3 months' duration

Physical examination showed a fairly nourished thin individual There was no cyanosis and no oedema of the legs Heart was enlarged, left border was 1" external to the mid-clavicular line and right border external to right lateral sternal line Presystolic thrill was felt in the mitral area, and systolic and diastolic murmurs in the pulmonary and aortic areas Tricuspid area was normal Occasional moist sounds were heard at the bases of both the lungs Liver was just palpable below the costal margin Blood pressure 140/80 There was no difference either in the pulse or in the blood pressure in both the arms

The patient had slight hoarseness of voice and laryngoscopic examination showed paralysis of the left vocal cord due to pressure on the left recurrent laryngeal nerve

Radiological examination on 7-2-44 (Figs 5 & 6) showed enlargement of the heart and abnormally prominent pulmonary conus R.A.O view with barium in oesophagus showed left auricular enlargement in addition Lungs showed basal congestion and right hilar shadow was prominent

Diagnosis Rheumatic heart, mitral stenosis, aortic regurgitation and abnormal pulmonary conus causing paralysis of the left recurrent laryngeal nerve

Case 3—V.L, Hindu, female aged 18 years, was admitted on 14-1-46 with a history of dyspnoea and general anasarca of 3 months' duration. She was married, 1st pregnancy ended in abortion in the 6th month, 2nd pregnancy delivered normal and the child is 1 year and 3 months old There was no history of rheumatic fever in the family

Physical examination revealed a fairly nourished individual with slight anaemia and general anasarca Heart was enlarged both to the right as well as to the left, the left border extending 1" external to mid-clavicular line Systolic and diastolic murmurs in the mitral, systolic murmur with accentuated 2nd sound in the pulmonary and systolic murmur in the tricuspid area were heard Aortic area was normal B.P was 94/70, and equal on both sides Lungs showed congestion of the bases, and liver was enlarged three fingers below the costal margin and slightly tender There was no irregularity in the

pupils to indicate irritation or paralysis of the left cervical sympathetic

Slight hoarseness of voice was present for the past 3 months Laryngoscopic examination on 18-1-46 showed paralysis of the left vocal cord due to left recurrent laryngeal nerve paralysis

Radiological examination on 18-1-46 showed enlargement of heart both towards right and left, prominent pulmonary conus, and enlargement of the left auricle in R.A.O view with barium in oesophagus (Fig 7 see plate I)

She was put on digitalis and diuretics by mouth and mersalyl injections once a week Signs of congestive heart failure disappeared, and a second radiological examination on 28-2-46 (Fig 8 plate II) showed diminished size of the heart including the left auricle Patient was examined again on 1-3-46 Although the voice appeared a little clear, laryngoscopic examination showed complete paralysis of the left vocal cord Electrocardiogram taken on 6-3-46 (Fig 9) showed ST 120 per minute, P positive in Leads I, II, III and indistinct in Lead IV, no abnormal prominence of P to indicate enlargement of the auricles, P-R interval 0.2 of a second, ST segment in Lead I elevated, T positive in Leads II, III, negative in Lead IV, S positive in Leads II, III, negative in Lead IV, S positive in Leads II, III, practically absent in Lead IV and right axis deviation

Diagnosis Rheumatic heart, mitral stenosis with insufficiency, and left recurrent laryngeal nerve paralysis The paralysis became more complete even though the left auricle became smaller in size

Case 4 -S.A., Hindu, female aged 28 years, was admitted on 15-2-46 for dyspnoea, palpitation and oedema of the legs of 2 years' duration She was married, has 4 children, the eldest was 14 and the youngest 4 years old During the last 3 months of the last pregnancy she had oedema which disappeared after normal delivery

Physical examination showed a fairly nourished individual with signs of congestive heart failure and filarial lymphangitis of the left leg Heart was enlarged, left border $1\frac{1}{2}$ " external to the mid-clavicular line and the right border just external to the right lateral sternal line Systolic murmur was heard in the mitral and tricuspid areas and 2nd sound was accentuated in the pulmonary area Rhythm was irregular and showed auricular fibrillation Liver was enlarged up to the level of the umbilicus, and lungs showed moist sounds over both sides more on the left B.P. was 112/80, and equal on both sides Pupils were normal and equal

Urine showed only a trace of albumin, but no casts Night blood was negative for filaria

There was hoarseness of the voice and laryngoscopic examination showed paralysis of the left recurrent laryngeal nerve Radiological examination on 4-3-46 showed enlarged heart, prominent pulmonary conus and enlarged left auricle in the right R.A.O view with barium in oesophagus

Electrocardiogram on 5-3-46 (Fig 10 plate II) showed auricular fibrillation, rate 90 per minute and right axis deviation There was no evidence of abnormally prominent fibrillatory waves

She was put on digitalis and diuretics by mouth and weekly injections of mersalyl. The patient showed improvement both of heart failure and paralysis of the left vocal cord. A second radiological examination showed diminution in the size of the heart including the left auricle.

Diagnosis Rheumatic heart, mitral stenosis and insufficiency with auricular fibrillation and left recurrent laryngeal nerve paralysis. The paralysis recovered after the decrease in the size of the left auricle.

DISCUSSION

Normally, the left auricle is smaller than the right and the walls are thicker. It is cuboidal in shape and extends to the right behind the right auricle. The roots of the pulmonary trunk and aorta are situated anteriorly and to the left. The posterior aspect of the left auricle forms the base of the heart. The auricular appendix can be seen projecting forwards at the left upper end overlapping the root of the left pulmonary artery. The left recurrent laryngeal nerve arises from the left vagus to the left of the aortic arch and hooks round below the arch just below the attachment of ductus arteriosus, ascends by the side of the trachea, and supplies all the muscles of the larynx except the cricothyroid (Johnston and Willis). The specimen (Fig 11) was dissected by Dr T. V. Mathew, Professor of Anatomy of the Andhra Medical College, to show the relationship between the left recurrent laryngeal nerve, arch of aorta, pulmonary artery and the left auricle.

Enlargement of the left auricle occurs posteriorly and to the right and can be visualised radiologically as a shadow within the shadow of the right auricle. In cases of extreme enlargement the right border of the cardiac shadow is formed by the left auricle. This dilated chamber directly or indirectly produces (1) difficulty in swallowing by pressure on the oesophagus, (2) consolidation of the left lower lobe of the lung by obstruction of the left bronchus, (3) feebleness of the pulse on the left side by indirect pressure of the left subclavian, (4) inequality of the pupils by pressure on the left cervical sympathetic and (5) hoarseness of the voice by pressure on the left recurrent laryngeal nerve.

Pressure on the oesophagus can be made out in the majority of the cases by radiological examination (right anterior oblique with barium in oesophagus) even though the symptoms are absent. In the earlier stages of clinically well defined mitral stenosis, radiological examination is negative in spite of electrocardiographic evidence of right axis deviation. In one of our cases (not included in the present series) enlargement of the left auricle was observed even though the signs and symptoms were only very slight. Symptoms of compression of the lung can be produced not only by an enlarged left auricle but also by the uniform enlargement of the heart or by pericardial effusion. Inequality of the pulse or of the pupils was not observed in any of our cases.

The four cases described above showed paralysis of the vocal cords by pressure on the left recurrent laryngeal nerve which supplies the left posterior crico-arteroid muscle. In Case (2) in addi-

tion to the enlargement of the left auricle, there was abnormally prominent pulmonary conus. Clinically, there was a possibility of mistaking this case for one of syphilitic aortic regurgitation and pressure on the left recurrent laryngeal nerve by aneurysmal dilatation of the aorta. Similar cases have been recorded (Osler and Gibson, loc cit). The presence of the mitral stenosis with the abnormal pulmonary conus confirmed the diagnosis of rheumatic mitral stenosis with commencing aortic regurgitation. This patient was seen 8 months later and the clinical symptoms were exactly the same. In Case (4) the paralysis of the vocal cords improved after treatment of congestive heart failure when reduction in the size of the left auricle could be made out. But in Case (3) the laryngeal paralysis became more pronounced although the signs of congestive heart failure disappeared and the left auricle diminished in size.

SUMMARY

(1) The literature of familial incidence, subcutaneous nodule and left recurrent laryngeal nerve paralysis in rheumatic infection is reviewed. These conditions occurring in association with mitral stenosis are described from a series of 728 cases of rheumatic heart disease observed in Vizagapatam (South India) during the last 12 years.

(2) Familial incidence was observed in 4 cases and in one family all the members were affected.

(3) Subcutaneous nodules were seen in one case and biopsy confirmed the diagnosis.

(4) Left recurrent laryngeal nerve paralysis was observed in 4 cases and the mechanism of its production is discussed.

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A NEW AMOEBICIDE FOR CHRONIC AMOEBIC DYSENTERY

H JACOBY, M D

Bhopal

Introduction — The frequent occurrence of relapses in the treatment of amoebic dysentery is the most depressing experience to patients and doctors alike. If the disease has been treated at the onset with a full and uninterrupted course of emetine injections, these patients have a fair chance of a permanent cure. If, however, the first treatment has not been carried out immediately after infection or was not patiently adhered to by allowing intervals or insufficient quantities of emetine in the treatment of the disease, then the chances of a cure are remote, the amoebae become resistant to emetine or the other amoebicidal drugs and the dreaded chronic stage of the disease ensues.

Consequently, instead of giving in this chronic condition emetine over and over again, the problem arises, which other drug may prove specific. A host of drugs has been tried out in the hope to fulfil this demand. We ourselves have tried among hundreds of patients the more common ones, separately or combined viz carbarsone, stovarsol, kurchi bismuth iodide by mouth, yatren as retention enema. But the same patients came again and again with their old complaints and with amoeba-findings in their stools, some times only a few days, some times a few weeks or months after completion of the respective treatment.

For this reason, we felt the urgency to look for a new remedy against this chronic, incapacitating disease. Since the oxyquinoline compounds, apart from emetine, appear to be among the more prominent amoebicides¹, we decided to try a new oxyquinoline preparation, by name "Amesanil Maltex", the properties of which are chemically far removed from emetine, the sulphonamides and the arsenicals. We, therefore, approached the importers² of amesanil for a trial supply. We administered amesanil to thirty patients suffering from chronic amoebic dysentery. Although it must be admitted that the time elapsed after the treatment is not sufficient to speak in the present series of cases of a permanent cure, the results achieved so far surpass all former methods of treatment. We feel that this fact calls for a report on this new amoebicide, since the inadequacy of our present treatment is widely admitted.

Properties of Amesanil Maltex — It represents chemically iodo-8-hydroxyquinoline-5-sulfonate of sodium, containing approximately 28% of iodine. Amesanil is a light yellow, inodorous powder, which dissolves in lukewarm water, forming a yellowish solution. It is non-toxic and does not irritate the tissues.

Treatment — The standard dosage adopted was 45 tablets of amesanil within seven days, viz, on the first day three tablets, on the second, third, fourth and fifth day six tablets and on the sixth and seventh day nine tablets. In no case was any other treatment

1 Morton T. C. St. C. British Medical Journal 4406 831, 1945

2 Dr. A. Wander (India) Ltd, Bombay

required only in one case a second course of amesanil, equal to the first one after an interval of a week

We judged the effect of the treatment by way of repeated microscopical stool examinations, before and after amesanil, furthermore by the disappearance of clinical symptoms, such as loose motions, tender colon, anaemia, loss of weight and finally by the relief of subjective complaints, such as griping pain, tenesmus, dysphagia

Our series of 30 chronic cases altogether consists of 20 patients, who had received other treatment before, as a rule with several more or less complete courses of emetine injections, followed by or in combination with oral carbarsone-, stovarsol-, or sulphonamide-administration and yatren-treatment as retention enema 10 patients had received no other specific treatment previous to that with amesanil, but were suffering for years from the symptoms of chronic amoebic dysentery, the origin of which was confirmed by us through the findings of amoeba histolytica in the stools

Results —The results of our trials with amesanil are a full success in the whole series of 30 chronic cases, those with previous treatment as well as those without There was not one failure, as far as the time of surveillance, i.e. two to three months goes All stools, repeatedly examined before treatment with amesanil, always showing amoebic cysts and often active amoeba also, became negative after one course of treatment, in one case after two courses The clinical symptoms arising from the amoebic lesions disappeared completely after treatment

Intolerance —No case of intolerance was encountered, there was no sign of iodism, no pronounced purgative effect, no vomiting sensation One patient only, after completion of his full course, showed swelling of his neck-glands, which disappeared after three days' local fomentation

Record of a chronic case —Mrs DK, 30 years old, had for the first time in 1936 dysentery with loose, blood and mucous containing stools and griping pain in the abdomen Amoebic dysentery was diagnosed and patient received injections of emetine But since she felt sick after each injection, she stopped the course after 5 injections altogether and refused to take injections ever since For the time being, she was apparently cured, but since then she suffered every year at least twice from an attack of the same disease, which she treated herself with castor oil emulsions, which gave her relief for a couple of months only This went on till December 1945, when patient was admitted to the hospital in a very emaciated and anaemic condition with griping pain tenesmus, loss of appetite and blood and mucous containing loose motions, six or seven a day We found in the stools entamoeba histolytica-cysts and vegetative forms also We carried out an eight days' treatment with oral carbarsol administration, 24 tablets altogether and simultaneously with daily yatren-retention-enema, each consisting of five tablets dissolved in 4 oz of water, to which a pinch of sodium bicarb was added At the end of this treatment, the stools were still found positive for entamoeba histolytica After an interval of 10 days, we managed to persuade patient to an emetine course of 8 injections, gr 1 each and

gave her at the same time daily an enterovioform-retention-enema for eight days. In spite of this treatment also, the stools were after a few days positive for *Entamoeba histolytica* again and the subjective complaints remained also. Consequently, we gave one full course of amesanil with 45 pills in seven days. Stools became negative at once, were so again on February 8th, 1946 and were still negative on March 20th, 1946. Patient has recovered strength, has got normal stools and complains of no pain any more, five months have passed now after completion of amesanil treatment without recurrence of the disease.

This record of a very chronic case is typical for many of our 30 cases. It shows, how too late a treatment with emetine and other amoebicides renders these cases resistant to such a treatment, but how quickly these patients respond to one course with amesanil only.

Summary —Amesanil Maltex appears to be the best of the oxy-quinoline group of drugs in the treatment of chronic amoebiasis and seems to play at least the same role of efficiency in chronic cases as emetine in acute ones. It is non-toxic and well tolerated in therapeutic doses.

The practice of treating chronic cases with emetine all over again, once it has failed to bring about cure, is to be discarded since it increases resistance to further treatment with emetine and renders them less amenable to other treatment with well-known drugs such as carbarsone, stovarsol, enterovioform, yatren.

Acknowledgment —My thanks are due to Dr. Bose, M.B. Pathologist, Prince of Wales Hospital, Bhopal, for his careful examinations of all stool specimens and to Messrs. Dr. A. Wander for the supply of Amesanil.

Addendum —Encouraged by the results with Amesanil in chronic amoebic dysentery, we tried the drug also on three acute bacillary dysentery patients. 45 tablets were given in the same way as above. Already after 4-5 days the dysentery stools subsided and at the end of the seven days course the cure was complete. No recurrence took place.

HYSTERECTOMY

Dr K M MASANI

In any large gynaecological unit, hysterectomy is a frequent operation. It is paradoxical, that each year number of contributions recommending conservative gynaecological surgery, appear in the medical press and at the same time the number of hysterectomies performed has also increased. It is not at all uncommon to find reports of several thousands of hysterectomies performed within a few years in foreign medical journals. In the gynaecological unit of the King Edward Memorial Hospital, Bombay, 206 hysterectomies were performed between January 1941 and December 1945. These operations were performed by Dr Daroovala, Dr Purandare or the author.

Out of 206 hysterectomies in this series, 135 were abdominal and 71 were vaginal. The report of these cases has been grouped into (1) indications, (2) anaesthesia and nature of operation, (3) post operative complications, and (4) general discussion.

ABDOMINAL HYSTERECTOMIES

Cases have been divided into two groups. (1) Hysterectomies done primarily for some disease or dysfunction of the uterus (Table 1), (2) Hysterectomies done secondarily during operation for the diseases of tubes and ovaries (Table 2).

Primary Indications

Fibromyoma Of 72 cases, 42 were multiparous, 26 married but sterile and 4 unmarried. The average age in these cases was 37.2 years. As many as 30 patients sought advice for a lump in the abdomen with or without any other symptoms. Abdominal pain and back-ache were present in 39, menorrhagia in 36 and menstrual irregularity other than menorrhagia in 30 cases. A record of blood count was not available in all these cases but in 11 cases there was marked secondary anaemia.

Functional Uterine Bleeding All the patients were multiparous and the age in 11 cases was 38.5 years. Menorrhagia from 1 to 6 years was the chief symptom and in all the cases there was secondary anaemia. In 2 cases, haemoglobin was below 50% and pre-operative blood transfusion was necessary. The uterus was found to be bulky in 8 of the cases, but in none of the cases cystic ovaries were palpated. In 2 cases pathological report was metropathia haemorrhagica, in 1 case placental polypus was reported, and in the remaining 8 cases the endometrium was found to be normal.

Chronic Endometritis and Chronic Metritis Of 4 cases, 1 was tuberculous endometritis and tuberculous salpingitis. This case, aged 23, had amenorrhoea of three months. At operation, dense adhesions were encountered and uterus with the tubal masses was removed with difficulty. This patient died of post-operative shock. In

A paper read at the 58th Meeting of the Seth C. S. Medical College and K. F. M. Hospital Staff Society, Bombay, on April 13, 1946 with Dr N. A. Purandare in the chair.

TABLE 1
Primary

Indications	No of Cases	Type of hysterectomy				Wertheim	Mortality	Remarks.
		Sub-total	Sub total & salpingo oophorectomy	Total	Total & Salpingo oophorectomy			
Uterine Fibromyoma	72	33	14	5	5		5	
Functional Hemorrhage	11	0	2				0	Case of tubercular disease of uterus and appendage
Chronic Metritis and Endometritis	4	2		2			1	One death after Wertheim one after pan hysterectomy
Carcinoma of Body of the Uterus	5	1	0	0		2	0	Case of an infant having sarcoma of cervix
Carcinoma of Cervix	6						2	Secondary haemorrhage from secondaries in vagina
Sarcoma of the Uterus	2			1			1	Stenosis of cervix and death from hyperpyrexia
Chlorion Epithelioma and Vesicular Mole	4	1	1		0		1	
Menometria	1	1					1	
Pelvic Prolapsed Polypus	1						0	
Adenomyosis	1	1	1				0	

TABLE 2
Secondary

Indications	Cases	Type of hysterectomy				Wertheim	Mortality	Remarks.
		Sub total	Sub-total & salpingo oophorectomy	Total	Total & Salpingo oophorectomy			
Ovarian Cysts	6		6				1	Death due to post operative shock
Ovarian Carcinoma	1		2			1	0	
Salpingo oophoritis	18	0	18				1	Death due to post operative Shock

the other 3 cases, painful profuse menstruation was the chief symptom and the uterus was found to be bulky and of hard consistency

Carcinoma of the Body of the Uterus Of 5 cases, 2 occurred in women over the age of 50 and post-menopausal bleeding was the chief symptom. The other 3 cases occurred in women before the onset of menopause, irregular bleeding was present, and their ages were between 40 and 45. As regards parity, 1 had seven full term deliveries, 1 four, 1 two, and 2 had one each. In 4 cases panhysterectomy was done, but in the remaining case there was infiltration of sigmoid colon, pelvic peritoneum and broad ligaments, subtotal hysterectomy followed by deep x-rays was done.

Carcinoma of the Cervix Carcinoma of the cervix is a very common condition met with in the out-patients department, but almost all of them are seen in late inoperable stage, and only 6 cases in the course of five years were seen in the early stages. Of these 6 cases, 2 were between 40 and 50 years of age, 2 between 30 and 40, and 2 below the age of 30. Regarding parity, 1 was sixth para, 1 fifth para, 2 third para and 2 had each one full term delivery. Irregular bleeding was present in all 6 cases, the shortest period of bleeding was for one day and the longest for ten months. In 2 cases a proper Wertheim's hysterectomy was possible and in the other 4 cases a panhysterectomy was done due to parametrial infiltration which was not evident on clinical examination. Post-operative blood transfusion was given in 4 cases. Two cases died of post-operative shock.

Sarcoma of the Uterus There were 2 cases in this series. One case was sarcomatous degeneration of a fibromyoma in a woman of 35 years who came under observation for rapid enlargement of the tumour upto the umbilicus. A panhysterectomy followed by deep x-rays was done. Other case was sarcoma botryoides, commonly known as the 'grape-like sarcoma of the cervix'. It occurred in an infant few months old, who had a blood stained vaginal discharge. On vaginal examination under anaesthesia, a vesicle was removed and section showed sarcoma. A panhysterectomy was done but the infant died of post-operative shock.

Vesicular Mole and Chorion Epithelioma Of 4 cases, 1 was a malignant mole in a female who came with three months' amenorrhoea and a tense, tender tumour increasing in size and reaching above the umbilicus. The uterus was found to be filled with blood. The other 3 cases were chorion-epithelioma. In 1 chorion-epithelioma occurred eight months after a full term delivery and in this case there were two secondary deposits in the vagina. A panhysterectomy was done, but severe, secondary haemorrhage from the secondary growths in the vagina on two occasions caused her death four weeks after the panhysterectomy. Friedman's test was done in all 3 cases and was found to be positive.

Haematometra In this case there was a bad vesico-vaginal fistula for which transplantation of ureters in the sigmoid was done. Some months later she returned for pain and a soft uterus was palpated per abdomen. It was then diagnosed as haematometra due

to a secondary stenosis of cervix. A subtotal hysterectomy was done but the patient got hyperpyrexia and died.

Ectopic This was done for an interstitial pregnancy.

Placental Polypus In this case a tongue-like spongy growth was seen protruding through the cervix. This had occurred three months after a conception. As the mass could not be removed a hysterectomy was done. In this case Friedman's test was negative.

Adenomyosis There was one case of this type. A bulky uterus with excessive bleeding and pain indicated the diagnosis.

Secondary Indications.—

Ovarian Cysts In 6 cases hysterectomy was done because carcinoma of the ovary was suspected at operation in 3 cases. In the other 3, there is no record regarding removal of the uterus with the cyst.

Ovarian Carcinoma There was pre-operative diagnosis of carcinoma and laparotomy was done. The uterus was removed with the ovarian carcinoma to minimise secondary recurrence.

Chronic Salpingo-oophoritis Of 18 cases, hysterectomy was done in some because both appendages required removal, in the other cases dense adhesions necessitated the removal of the uterus with the inflammatory masses.

Nature of Operation In this series of 135 abdominal hysterectomies there were 13 deaths, a percentage of 9.6. This appears to be an unduly high percentage but analysis of Tables 1 and 2 will show that 8 deaths occurred in cases where hysterectomy was associated with other complicating factors, while it is difficult to analyse the remaining 5 deaths, which occurred in cases of fibromyoma, as there is no detailed record of the causes of deaths.

Subtotal Hysterectomy Of 114 cases of subtotal hysterectomies, 68 were purely subtotal and 46 subtotal with removal of appendages. In most cases of subtotal hysterectomy coning of the cervical stump was done to remove most of the cervical mucous membrane and at the same time to preserve the attachments of the utero-sacral and lateral cervical ligaments. When hysterectomy is necessary for primary non-malignant indications, such as fibromyoma, functional haemorrhages and chronic metritis, it is my opinion that a total hysterectomy is not higher than subtotal. Removal of the cervix eliminates future risk of malignancy. Persistent chronic cervical discharge from the cervical stump is at times resistant to treatment. The disadvantage of prolapse of the vault of the vagina after total hysterectomy is minimised by fixing the stumps of the uterosacral ligaments to the vaginal incision.

Panhysterectomy There were 4 cases of vesicular mole and chorion-epithelioma (Table 1) and in only 2 cases panhysterectomy was done. Of the other 2, 1 was a case of haemorrhage in a vesicular mole and in the other case diagnosis of chorion-epithelioma was made on pathological examination of the specimen.

Of 5 cases of carcinoma of the body panhysterectomy was done in 4, and subtotal hysterectomy in the remaining case was done because of the infiltration of sigmoid colon, pelvic peritoneum and broad ligaments.

TABLE 3 —Indications for vaginal hysterectomy and type of operation

Indications	No of Cases	Mayo-Ward	Schnauta	Subtotal Vaginal Hysterectomy	Total Vaginal Hysterectomy	Mortality
Prolapse	27	18			9	1 died of shock
Functional haemorrhage	29			3	26	
Fibromyoma	4				4	
Chronic metritis	4			1	3	
Secondary haemorrhage after D & C.	1				1	
Malignancy	6		2		4	

VAGINAL HYSTERECTOMIES

Indications It is obvious from Table 3 that all the indications for vaginal hysterectomy are primary. Wherever there is a complicating factor, it is much better to do an abdominal operation and after exploration decide the exact nature of operation.

Prolapse of the Uterus Vaginal hysterectomy is indicated in women over the age of 40 in whom either the cervix is considerably elongated with a second degree of uterine prolapse or where there is complete procidentia. It is particularly indicated when the cervix is badly eroded or lacerated due to previous childbirth. In this series there were 27 cases. In 17 there was 3rd degree of uterine prolapse, while in the other 10 the prolapse was of 1st or 2nd degree with cystocele and prolapse of posterior vaginal wall. In deciding hysterectomy four associated conditions were taken into consideration: (1) menstrual irregularity, (2) elongation of cervix, (3) erosion and ulceration of cervix, (4) degree of cystocele. In several cases two or three of these complicating factors were present.

Functional Haemorrhages

The age and parity in 29 cases is given below in Tables 4 & 5.

TABLE 4 —Age in 29 cases

Ages	No. of Cases
Below 35	2
Between 35 & 40	22
Above 40	5

TABLE 5 —Parity in 29 cases

Parity	0	1	2	3	4	5	6	7	8	9	10	11
No. of cases	1	0	3	5	4	4	4	3	3	1	0	1

The chief menstrual irregularity in 18 cases was menorrhagia and all the cases had secondary anaemia. In the other 9 cases the periods were frequent and irregular, but secondary anaemia was not present. It is therefore evident that gross menstrual irregularity in women over 35 and who have had several full term deliveries was the chief indication for this operation. As 24 cases were below 40 years of age deep x-ray or radium would have been an unsuitable method for stopping menstruation.

It must be admitted that curettage was not given a preliminary trial for the following reasons. Hospital class of patients do not

attend regularly and particularly after an operation that has failed to relieve their symptom. Another reason was that in most of the cases the patients did not wish to conceive any further and that together with the irregularity were the deciding factors. Anaemia was a prominent symptom in 18 cases and it appeared unwise to treat them by palliative methods.

Malignancy of Uterus There were 6 cases where a clinical pre-operative diagnosis of malignancy was made. In 4, carcinoma of the cervix and in the remaining 2 carcinoma of the body were suspected. Of the 4 cases of suspected carcinoma of the cervix, 2 were squamous celled carcinoma diagnosed before operation by biopsy, but the examination of the removed specimen in the other 2 cases showed vascular erosion. Of 2 clinically suspected cases of carcinoma of the body, one was an adenocarcinoma and the report of the other specimen was cystic dilatation of the endometrial glands which showed no malignant change.

It may be asked why pre-operative biopsy was done in 2 cases only. The reason is that hospital class of patients often ask for a discharge if they are kept waiting for some days for a biopsy report. Some patients in whom biopsy was done went away against medical advice before pathological report could be obtained. It has, therefore, been my practice recently that if there is a clinical suspicion of malignancy and the patient is not inclined to wait, a hysterectomy is done without a previous biopsy.

Fibromyoma Fibromyoma was submucous in 3 cases and in 1 there were multiple intramural growths. The size of the uterus in 4 cases was not larger than 10 weeks' pregnancy. In all the cases menorrhagia was the chief symptom. In 2 cases, curettage for menorrhagia caused continuous bleeding after the operation and digital exploration of the uterine cavity palpated small submucous growths.

Vaginal operation for removal of fibromyoma is only undertaken if the bulky uterus is mobile and there is no evidence of any adhesions and when the size of the uterus is not larger than 10 weeks' pregnancy. Although larger ones are often removed by the vaginal route I prefer to remove such large growths by the abdominal route as considerable difficulty occurs while removing them vaginally.

Chronic Metritis In all 4 cases menorrhagia and irregular bleeding were the chief symptoms. The uterus in all of them was found to be bulky, of smooth surface and very hard in consistency. All 4 cases were parous, 1 had six, 2 seven and 1 nine previous pregnancies.

Secondary Haemorrhage after Curettage In this case curettage was done in a case of incomplete abortion which was wrongly diagnosed before operation as metropathia haemorrhagica. She was plugged for 24 hours and on removal of the plug she started bleeding again. She was plugged again and the plug was removed 48 hours later. Soon after removal of the plug the bleeding commenced and a hysterectomy was done. Examination of the specimen showed that the curettage had damaged and thinned out the uterine wall in one place and a vein had been opened up. Fortunately she was 39 years of age and had two living children. This patient had a very stormy convales-

cence and had temperature for nearly 3 months, staphylococcus aureus was found on several occasions in blood culture. She eventually recovered after a very stormy convalescence of 12 weeks.

Nature of Operation Table 3 shows the nature of operation done. In 18, Mayo Ward's operation was necessary for marked uterine and vaginal wall prolapse. In 2 cases, Schauta operation for carcinoma was diagnosed by pre-operative biopsy. It is seen that in 4 cases, 3 of functional haemorrhage and 1 of chronic metritis, subtotal hysterectomy was done. In the remaining 47 cases total hysterectomy was performed.

Mayo Ward operation is a very satisfactory procedure for complete procidentia in women nearing the menopause, particularly when there is a large cystocele. Not only is the prolapse effectively cured but also the danger of carcinoma or senile endometritis is eliminated. This operation is superior to Manchester operation and has been my choice since the last three years.

Schauta Operation This was done on two occasions, and with sufficient practice and proper selection of cases is a very satisfactory operation for carcinoma of cervix with less shock and low primary mortality.

Subtotal vaginal hysterectomy was done in the above mentioned 4 cases but since the last two years total hysterectomy has been the routine method as there is a potential danger of carcinoma developing in the cervical stump. The disadvantage of prolapse of the vaginal vault after total hysterectomy is minimised by anchoring the stumps of the utero-sacral and lateral cervical ligaments to the vagina during final suturing of the vaginal incision.

Post-Operative Complications

It will be evident by comparison of Tables 6 and 7 that post-operative complications are more frequent and of more serious consequence in abdominal operation.

TABLE 6
Post operative complications in abdominal hysterectomies

Nature of complications		No. of cases	Percentage
Shock		20	4.2
Pyrexia		23	17.0
Urinary			
(a) Retention of urine	21		
(b) Cystitis	9		
(c) Pyelitis	14	44	32.6
Gastro intestinal			
(a) Distension	18		
(b) Diarrhoea	2		
(c) Vomiting	10	30	22.2
Respiratory			
(a) Bronchitis and pneumonia	20		
(b) Massive collapse	0	20	14.8
Secondary haemorrhage		1	0.74
Secondary wound infection		17	12.6
Urinary fistula			
(a) Uretero vaginal	1		
(b) Vesico vaginal		1	0.74
Post operative hernia		1	0.74

TABLE 7

Post-operative complications in vaginal hysterectomies

Nature of complications		No of cases	Percentage
Shock		3	4.2
Pvrexia		18	25.3
Urinary			
(a) Retention	4		
(b) Cystitis	4		
(c) Pyelitis	6	14	19.7
Gastro intestinal			
(a) Distension	8		
(b) Diarrhoea	1		
(c) Vomiting	4	13	18.3
Respiratory			
(a) Bronchitis and pneumonia	4		
(b) Massive collapse	0	4	5.6
Secondary haemorrhage		1	1.4
Urinary fistula			
(a) uretero vaginal	10	1	1.4
(b) Viscio vaginal	1		
Foul vaginal discharge		26	36.6

Post operative shock in abdominal cases was 14.8% while it was only 4.2% in vaginal cases. This comparison is, however, erroneous because only mobile and straightforward cases were operated upon vaginally, while there were several abdominal cases with associated complications requiring a more prolonged and severe operation. Timely blood transfusion helped recovery from shock in several cases.

Urinary complications in abdominal cases were 32.6% while in vaginal operations they were 19.7%. This lower percentage in vaginal operations was partly due to routine use of self-retaining catheter in all vaginal operations reducing the number of cases of post-operative retention of urine.

Gastro-intestinal complications in abdominal cases was 22.2%, while it was 18.3% in vaginal operations. As there was no handling of abdominal viscera during vaginal operations, gastro-intestinal symptoms were not so serious. Although the percentage 18.3 is comparatively high it must be noted that distention and vomiting were of much less severity in these cases and were relieved by simple measures.

Respiratory complications The percentage in abdominal cases was 14.8 and in vaginal cases 5.6. Accurate data is not available for evaluating this difference, but it is likely that in some abdominal operations which lasted for more than an hour general anaesthesia was supplemented on spinal injection and this dual anaesthesia increased the incidence of respiratory complications in abdominal cases. The effect of spinal anaesthesia lasts for a longer time in vaginal operations and general anaesthesia is seldom required to be supplemented.

Secondary Wound Infection In this, all cases from small stitch abscesses to complete breaking down of the wound are included and only in 4 cases secondary suturing was necessary.

Urethral Fistula One case of uretero-vaginal fistula occurred after a total abdominal hysterectomy which spontaneously healed after 3 weeks. Implantation of the damaged ureter was being considered when the leakage rapidly diminished and the fistula closed. A case of vesico-vaginal fistula occurred after Mayo Ward operation for prolapse. A self-retaining catheter was kept in for some weeks and the fistula healed.

Secondary Haemorrhage One case recorded in abdominal hysterectomy was that of chorion-epithelioma with secondaries in the vagina. The secondary growths in the vagina caused very severe secondary haemorrhage on two occasions. One case in vaginal operation was following vaginal hysterectomy and the bleeding was from the vaginal incision.

GENERAL DISCUSSION

Uterus is an essential organ having varied functions, most important of which are menstrual, reproductive, psychological and metabolic. All these functions are inter-related and have an important relationship with the endocrine system. Hysterectomy is performed most frequently for disorders of menstrual function, and very little attention is paid by the gynaecologist to the upset of psychological and metabolic functions caused by the removal of uterus. Sexual function is taken into consideration and hysterectomy is seldom performed in unmarried or married females below the age of 35.

Reports from various centres giving indications, technique of operation and post-operative complications frequently appear, but there are very few contributions which deal with alterations in psychological and metabolic functions following this operation. Such a study should be jointly undertaken by a psychiatrist, biochemist and gynaecologist. It is unfortunate that the gynaecologists have inclined more towards surgery during the last few decades and it is still more unfortunate that surgeons practising general surgery at times perform this operation disregarding the important functions of this organ.

In recent years it has been pointed out that ovaries left behind after hysterectomy undergo atrophic changes because the activity of the ovaries is dependent on the presence of the endometrium. If this is confirmed by further studies, the indications for the removal of uterus will require revision.

Each year clinical, biochemical and endocrine researches attempt to throw more light on dysfunctional uterine bleeding and it is to be hoped that conservative means will be available in future for correcting such dysfunction and it will then be not necessary to perform hysterectomy for this indication.

Similarly, attempts are being made to control the growth of fibromyoma by injections of the male hormone. If such attempts are successful fewer hysterectomies will be necessary for this common indication.

DISCUSSION

Dr B N Purandare said that Dr Masani had emphasised the need for performing a still greater number of total abdominal hysterectomies in place of abdominal sub total hysterectomies. He emphasised that two adverse effects of this procedure had to be realised the comparative higher mortality in total hysterectomy and the tendency for the vaginal vault to prolapse after the operation. He said that in his series of 428 hysterectomies the mortality rate for total abdominal hysterectomy was 2.5% compared to 0.52% for the sub-total abdominal type. In his opinion this adverse effect could be minimised by substituting the vaginal total hysterectomy which in his series had a mortality of 0.56% and the prolapse of the vault could be avoided by fixing the round ligament and the utero-sacral stumps to the vaginal vault. The modification which he found useful was to leave behind the vertical column of the lateral cervical vaults in total hysterectomy and these could then be united in the middle line so as to maintain the integrity of the pelvic floor with the danger of injuring the ureter and the amount of surgical shock minimised. In his opinion the use of the vagino-abdominal method was a more useful procedure as it shortened the duration of the operation and with less shock. He added that the deeper structures in the pelvis namely the lateral cervical ligaments, the vaginal vault and the lateral angle of the vaginal could be dealt with from below the vaginal vault closed per vaginum followed by the abdominal removal of the uterus. In his experience the operation was not followed by shock even in the presence of adhesions and restricted mobility of the cervix the result of previous parametritis. He concluded that in cases of uterine fibroids enucleation of the tumour carried out by the various modifications, the organ could safely be removed as evidenced from his series of over 200 operations of vaginal hysterectomies.

He was glad that Dr Masani discussed in detail the case of vaginal hysterectomy which had various infective complications in the post-operative period and which had a previous D & C done prior to vaginal removal. He noted in his series similar effects if vaginal operations were carried out immediately previous to vaginal hysterectomy even if it was a minor one like D & C or exploration of the uterus. In fact, the only case he lost of vaginal hysterectomy had exploration of the uterus previous to the major operation. The use of routine biopsy could be carried out especially in cancer body case in K E M Hospital but it was found that some of the cases were lost as patients failed to return to the hospital after the biopsy report was received. Therefore they preferred to remove the uterus and have the whole uterus for microscopic study rather than wait for the biopsy report.

As regards the post-operative complications the incidence of shock as far as Dr Purandare had observed was much less after vaginal removal than after abdominal hysterectomy. The gastro-intestinal complication as shown in the statistics were practically equal in both the methods but this might be due to the effect of spinal anaesthesia for if the vaginal operation is carried out under local anaesthesia these were absent. He had reduced the incidence of the secondary haemorrhage in vaginal hysterectomy by the use of the mattress sutures to close the vaginal vault.

He said that removal of the uterus should not be associated with psychological disturbances so long as the blood supply to the ovary had been preserved. This could not be avoided in radium and X-ray treatment which may be expected to be followed by severe menopausal disturbances. The atrophy of the ovary following the removal of the uterus is a finding without any basis and could be disproved by animal experiment by selecting the animal which had a separate blood supply to the tube and the ovary. In such animals the removal of the uterus is not followed by the atrophy of the ovary which continues to have its own blood supply.

He then gave the results of 428 operations of hysterectomy performed by him at the K E M Hospital cases and in private

Total number of Hysterectomies 428 (Mortality 0.7%)

(K E M 125 (Mortality 0.8%))		Private 303 (Mortality 0.56%)	
Abdominal		Vaginal	
227 (53%) (Mortality 0.88%)		201 (47%) (Mortality 0.5%)	
Sub-Total		Sub-total	
189 (83.3%)		25 (12.4%)	
(Mortality 0.52%)		(Mortality Nil)	
Total		Total	
38 (16.7%)		178 (87.6%)	
(Mortality 2.6%)		(Mortality 0.56%)	
K E M	Private	K E M	Private
55	134	12	20
		8	17
		50	126

Dr C M Mehta said that the vaginal hysterectomy was preferable to the abdominal one as the operation was simpler the complications less severe and the convalescence shorter in the former operation except when there were adhesions or tumours in the uterus. He further said that metropathia in younger subjects was better treated by vaginal hysterectomy and in the menopausal age by radium.

Dr K A J Lalkaka emphasized the need of preparing the patient psychologically prior to the operation to obviate the subsequent mental disturbance supervening on the loss of a much prized organ.

Dr J N Karande drew attention to the need of an efficient pre-operative and post-operative treatment and the necessity of a laboratory attached to the gynaecological wards.

Dr L H Athle spoke on the use of radium therapy in malignant conditions of the uterus.

Critical Notes and Abstracts

EXHAUSTION SYNDROME IN EXCITED PSYCHOTIC PATIENTS-

Shulack, N R (Am J of Psychiatry, 102-4, Jan 1946, pp 466-475) describes the clinical features, pathological physiology and rational treatment of the syndrome. The paper emphasizes the seriousness of the syndrome. Up to May 1944, 403 cases of acute exhaustion death have been reported in the literature, of which 158 cases of acute manic depressive psychosis, 74 of schizophrenic catatonia, and 171 untabulated or mixture of diagnosis. The post-mortem findings were all negative except for general visceral and encephalic congestion. Clinically, the consistent findings in these patients have been a period of antemortem excitement, derangement of the thermal control mechanism, rapid pulse and low blood pressure with termination by sudden complete inhibition of the cardiac cycle.

The clinical features of the syndrome are

- 1 *Sustained motor and mental excitement* with continual activity for a period usually from 2 days to 2 weeks
- 2 *Rapid thready pulse*
- 3 *Rapid loss in body weight*
- 4 *Profuse clammy perspiration*
- 5 *Fall in blood pressure and pulse pressure*
- 6 *Pyrexia*, usually from 100° F to 104° F if death does not occur, hyperpyrexia up to 110° F or higher prior to death

Many of these patients are young, had previously led useful lives and had developed psychoses very shortly prior to the excitement period. The clinical picture of a typical case is as follows:

A young individual, in the 2nd or 3rd decade of life, becomes restless and excited. This psychomotor activity increases and is accompanied by euphoric hilarity or fearful anxiety in response to extrospective or introspective pressure of ideas. Work and duties are neglected. Impulsive or responsive aggressiveness increases. The individual breaks equipment or furniture or assaults his neighbours, apparently without reason. He is admitted to the hospital. The excitement and restlessness continue day and night, with only momentary respite. Excitement increases until it becomes a continual maniacal furor, in which the individual will tear off his clothes, tear the bed clothes to strips, take the bed apart, rip the mattress to pieces, bang and pound almost rhythmically on the walls and windows, dash wildly from the room, assault anyone in reach and run aimlessly, and without apparent objective, from one end of the room to the other. The pulse becomes rapid even in the periods of momentary rest. Weight loss becomes marked. Perspiration is profuse and continuous. The blood pressure falls, and the pulse becomes thready. Fever is then noted. Early in the furor it ranges around 100° F (R). When confined to a room, the patient will thrash against the wall or butt his head against it. If placed in restraint, either in a continuous tepid tub or in bed, (in pack or sheet), the patient will strain ceaselessly against the restraint in an attempt to tear

out and maintain his externally objectiveless activity. Fever increases, the pulse becomes more thready and rapid, blood pressure falls further, perspiration drips continually, the tongue becomes dry and furred, the skin becomes flushed and feels hot to the touch. After varying periods of excitement from hours to days, the temperature may rise to 105° F (R), or 107° F (R), or even 110° F (R). The skin may become pale or cyanotic and suddenly all activity ceases, respiration and cardiac activity stop, and the patient is dead. This end may come so suddenly that the attending psychiatrist is left with a chagrined surprise, as if to say to himself, "What happened? Why did this patient die?" "No apparent physical disease was present!" "What could I have done to help him?"

The chief features of the pathological physiology are —

- 1 *Vagal hypertonia*—Over irritation of vagal nerve or centre or carotid sinus reflex
- 2 *Psychic and Emotional Tension*—Overactivity of hypothalamic centres with resultant autonomic imbalance
- 3 *Toxaemia*—Excessive production of lactic acid, histamine and H-substance of Lewis, producing vasodilation and peripheral vascular stasis and circulatory failure
- 4 *Sodium Loss*—Through excessive perspiration. High potassium ratio, enhancing the action of histamine, and producing exhaustion shock
- 5 *Disturbed Acid-base Balance*—
- 6 *Sudden Atony of the Circulatory System*—

Shulack has treated 7 cases successfully on the following lines —

- 1 *Sedation*—The constant muscular activity produces an accumulation of catabolites in the peripheral tissues with resulting vasodilation. This is checked by barbiturates (1 Gm daily, is found most useful e.g. Sodium amytal intravenously 0.5 Gm twice a day, or 0.4 Gm three times a day orally). Tepid bath or cold sheet is occasionally found to be useful.
- 2 *Tube feeding* is necessary when the patient does not take sufficient food and water by mouth. Liberal well balanced diet, minerals, vitamins and water must be given, orally or by tube feeding if necessary, twice or thrice a day. Each pint of food should contain 2 eggs, 8 oz of milk, 5 gms of Sodium chloride, 1 oz of sugar, 2 oz of citrus fruit juice, 2 oz of beef extract, and powdered vitamins (thiamine chloride 10 mg, Niacine 50 mg, and ascorbic acid 50 mg).
- 3 *Fluids* 2000 to 4000 ml of fluid in 24 hours should be supplied, of these 1000 ml may be given intravenously as 5% glucose saline twice a day.
- 4 *Salt* 10 Gm of salt in feeds, the rest in saline infusions.
- 5 *Adrenal cortex extract*—to combat shock eschatin (50 dog units per ml) 1 to 2 ml three times a day intramuscularly.
- 6 *Hypopyrexia* starts some days after the beginning of loss of body weight, and is as yet inadequately explained. Whether it is due to dehydration, early shock, increased psychomotor

activity, or central neural damage of the heat regulating centre, or a combination of any or all of these, is not yet clear. At any rate it is an indication of the onset of the exhaustion syndrome and it is the first indication for starting the above therapy immediately. Hyperpyrexia above 105°F (R) indicates an extremely grave condition usually resulting in death.

Adequate treatment is necessary for one to two weeks, but it may take longer, as long as 6 weeks. Subsidence of pyrexia is the best index of improvement from exhaustion.

(Recently the reviewer had two patients suffering from this syndrome under his care who developed femoral thrombosis. Vascular stasis, low blood pressure and toxæmia were probably the cause. In both these patients the temperature was brought down to normal by penicillin, 40,000 U/3 hrly for 5 to 8 days. Both made a clinical recovery from the exhaustion syndrome on following the above line of treatment.)

Original Contributions

RHEUMATIC LUNG, IMITATING MILIARY TUBERCULOSIS

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The steadily increasing number of clinical syndromes of allergic origin, manifested—partly at least—in the lungs, such as Loeffler's syndrome, tropical eosinophilia and bagasse disease, as well as the growing interest in so-called rheumatic pneumonia, of which the microscopic appearance is much better known than the clinical symptomatology, might justify the publication of the following observations in some detail, the more so as they confirm that close relations exist between allergic and rheumatic pulmonary processes

Case Report Mr P N K, (Ser No 4942 A) aged 30 suffered from pneumonia in 1916 and from rheumatic fever in 1926. In 1938 he noticed subfebrile temperatures and got himself admitted to a lung sanatorium where he remained from April 26 to September 25. For 10 weeks he showed hardly any rise of temperature and gained 13 pounds of weight, none of the examinations, performed there, revealed any tubercular lesion. When he was about to leave the sanatorium, a second attack of rheumatic fever developed which lasted for about one month. Several joints were involved, showing redness and swelling to such an extent that he was unable to move, remittent fever up to 102°F lasted for a fortnight, up to 101°F for another 10 days (August, '38). From September 28, 1938, upto February 2, 1939, he was an in-patient in another hospital because of vague pains in his shoulders and stiffness of wrists and finger joints. Throughout this time he was practically afebrile and gained 20 pounds of weight, having lost 23 pounds during the rheumatic attack. According to his case histories heart and kidneys were not affected at any time. In March, 1939, at a university hospital the following blood picture was found: red blood cells 5,140,000, haemoglobin 105 per cent (15.8 gm), leucocytes 9,520, polymorphs 65 per cent, lymphocytes 34 per cent, eosinophils 1 per cent. The same year his tonsils were removed because of chronic tonsillitis. In 1942 he had a severe attack of typhoid. In 1943 a skiagram of his lungs (fig 1), taken in Bombay, showed normal conditions. By the end of April, 1944, he had a short febrile attack in Karachi, diagnosed as 'flu'.

On May 19, 1944, the illness started which we wish to report. On this day he returned from Karachi to Calcutta where he arrived with 101.5° F, apart from headache and a dry cough, there were no complaints, especially no signs of asthma at any time. During the first 3 weeks of this febrile condition two sputum examinations, a urine culture and a Widal test were performed—all with negative result.

A doubtful blood examination, four days after the onset of fever, showed an eosinophilia of 24 per cent without estimation of the total leucocyte count, but less than a fortnight later eosinophils made up only 12 per cent of 10,500 leucocytes, a percentage which never was exceeded during the course of this illness. In spite of the administration of sulpha drugs, the fever continued, frequently reaching 102° in the evening with normal temperatures in the morning. The first skiagram of the lungs since the onset of this fever was taken on June 21, 1944 (fig 2), it showed numerous opacities of lentil size, distributed through both the lungs, predominantly in the lower two-thirds of the lung-fields. The diagnosis of tuberculosis seemed almost certain, while one physician suspected tropical eosinophilia. About a fortnight later patient was admitted to the tuberculosis sanatorium, Jaipur, where after thorough examination the suspicion of pulmonary tuberculosis was confirmed, although repeated sputum examinations failed to show acidfast bacilli. At this time, 5 weeks after the first skiagram was taken in Calcutta, another one was made here (July 29, fig 3), which not only confirmed the previous findings of an almost miliary dissemination but even showed an increase in the number of these opacities so that both the lung-fields had a ground glass appearance, even the apical parts which in the previous picture were much less involved, now were studded with small exudative infiltrates.

On August 8, 1944, patient was admitted to our hospital where he remained up to October 23, 1944. Physical examination of the lungs showed no dulness on percussion, normal V R. and V F, no bronchial breathing anywhere, some dry rales and a few rhonchi represented all the adventitious sounds. In spite of daily repeated examinations, crepitation or consonant rales were never found. The heart showed nothing abnormal and remained unaffected, clinically and radiologically, throughout the whole illness. Liver and spleen were not enlarged. Urine and motion did not contain any pathological elements. Pulse was of good quality, its rate varied strictly with the temperature, from about 80 in the morning, when the temperature was normal, to 120 and even 130 in the late afternoon when his fever rose to 101° or 102°. Blood pressure 115/80 mm Hg. The white cell count on admission was 12,000 with 71 per cent neutrophils, 21 per cent lymphocytes and 8 per cent eosinophils. Sedimentation rate was $\frac{50/30 \text{ min}}{100/60 \text{ min}}$ (Westergren). The sputum was almost daily examined, several times by the antiformin concentration method, and gave always a negative result for tubercle bacilli, nothing but the usual bacterial flora was present, neither eosinophil leucocytes nor Charcot-Leyden crystals were ever found.

Although we had not much doubt that patient suffered from a tuberculosis affection, we gave him three novarsenobillon injections to exclude an atypical tropical eosinophilia, each of them was followed by severe headache, vomiting and a still higher rise of temperature with no beneficial effect whatever. Patient had lost 25 lbs of weight and complained about almost complete anorexia and weakness, his only other complaints were cough with very little expectoration and night sweats. A skiagram, taken on August 15 (fig 4), showed a still denser mottling so that hardly any normal lung tissue remained visible and his leucocyte count was 11,000 with 11 per cent eosinophils while the sedimentation rate rose to 60/100 (Westergren). On August 22, with a temperature of 101° patient felt weaker than usually and deeply depressed. To give him some relief by lowering his fever, this evening one aspirin-phenacetine-caffeine powder (aspirin gr 5, phenacetine gr 2, caffeine citr gr 1) was given which brought down the temperature to subnormal by the next morning. Under continued antipyretic treatment (one-half of such an

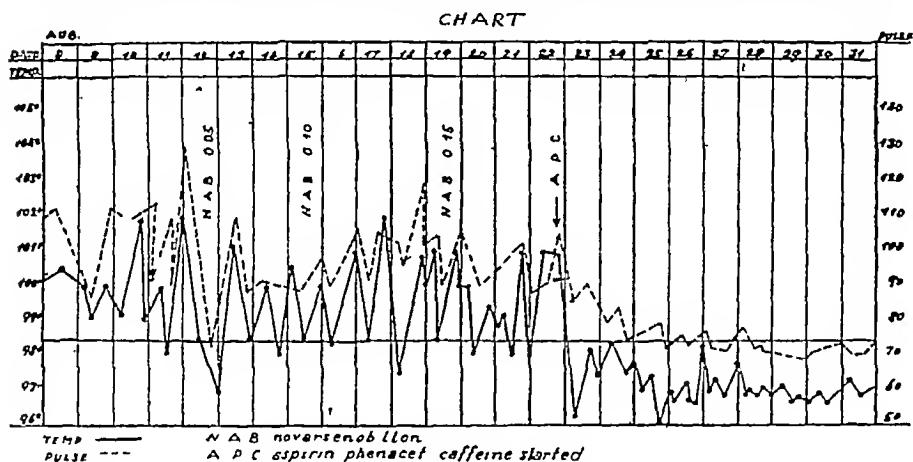


Chart I

aspirin-phenacetine-caffeine powder, thrice a day) his temperature remained normal from this day on (see chart), in fact, for the last one and a half year he never had the slightest rise of temperature, although he took the last antipyretic dose on September 20, 1944. Apart from some iron-liver tonics, he had no other treatment in hospital or afterwards.

The almost incredible improvement of the patient's general condition which set in about one week after starting the aspirin-phenacetine-caffeine medication was fully confirmed by radiological findings and his blood condition. On Sept 14, after 3 weeks of this treatment, the sedimentation rate was 18/42 and the skiagram of Sept 15, (fig 5) showed a very considerable clearing of both the lung-fields due to the disappearance of many of the opaque spots which from June 21 to Aug 15 were seen in increasing numbers in three skiagrams, his weight had increased by 8 lbs. At this time patient complained about some pain in the knees which induced him to stay in bed for about 10 days.

longer than we advised. A fortnight later, on 28-9-44, when his appetite hardly could be satisfied and another 5 lbs had been gained, the leucocyte count which up to now always was between 10,500 and 16,000, dropped to 5,000 with 10 per cent eosinophils, the sedimentation rate, which on the day when the first aspirin-phenacetine-caffeine powder was given had been 60/100, to 12/32 (Westergren). A skiagram, taken on Oct 5 (fig 6) showed instead of ground glass appearance due to a miliary-like dissemination only increased lung markings, especially near the hilum and in the basal areas. The white blood picture on 14-10-44 showed practically no change compared with that of Sept 28, the sedimentation rate a further slight reduction to 10/25. When he was discharged on 23-10-44, his weight had increased from 104 to 120 lbs within just two months. We examined him afterwards on various occasions, the last time on 22-2-45 when his skiagram (fig 7) was normal, except for some peribronchial thickening in the right lower lobe, his weight 135 lbs and his general condition better than ever.

DISCUSSION

Pulmonary tuberculosis which seemed the most probable diagnosis at the time when the patient suffered from high fever, lasting for more than three months, and the X-ray photos almost seemed diagnostic of a diffuse haematogenous dissemination, resembling a miliary tuberculosis, was excluded by the sudden change in the course of the illness which in one month led from a desperate looking condition to clinical health, moreover seventeen sputum examinations, about one-half of them performed by the anti-formin method, between Aug 9 and Sept 15, 1944 failed to show tubercle bacilli.

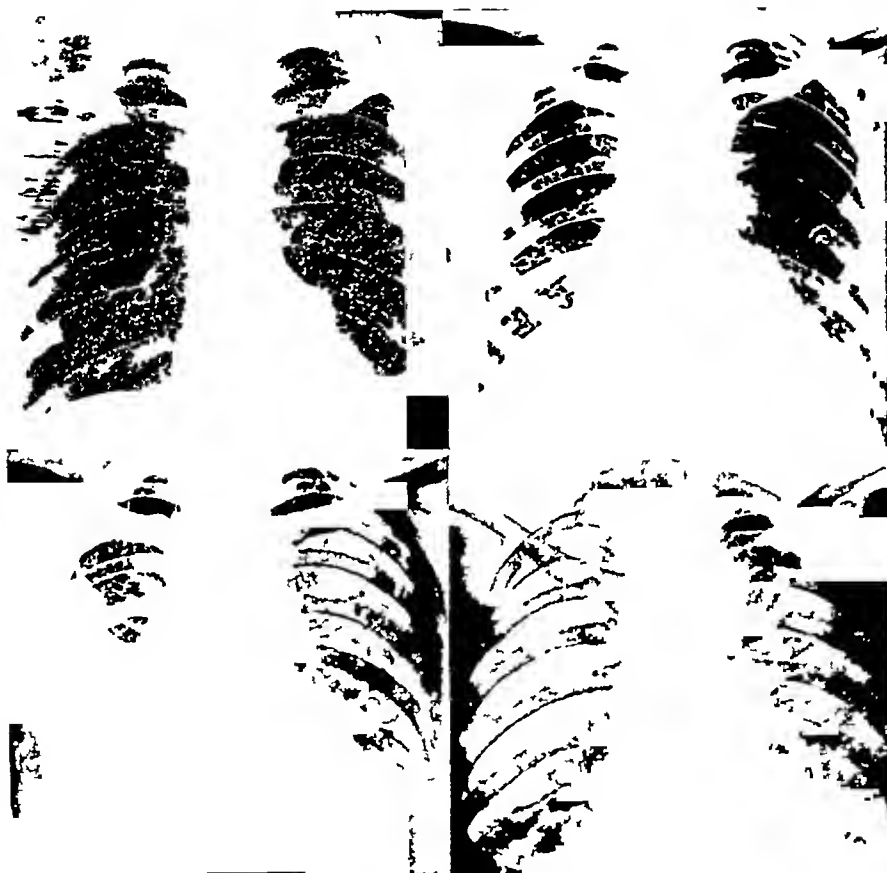
Loeffler's syndrome (Loeffler, 1936) or the transient eosinophilic infiltration of the lungs (Edit, 1944) is characterized, as the name indicates, by a far shorter duration, higher eosinophilia and a radiological lung picture which, although somewhat varying in appearance, never resembles a miliary tuberculosis.

Tropical eosinophilia (Frimodt-Moller & Barton, 1940, Weingarten, 1943) differs in every essential feature from the case under discussion. Initial short and usually moderate rise of temperature, asthma-like attacks, considerable leucocytosis, extremely high eosinophilia and prompt response to organic arsenicals characterize tropical eosinophilia. Long lasting high fever, absence of asthma complaints, only slightly increased leucocyte count and moderate eosinophilia, no response to arsenicals but almost immediate improvement on salicylates in our case rule out tropical eosinophilia.

If the prompt response to salicylates is taken as a distinctive feature, perhaps leading to the right diagnosis, one has to think of a rheumatic lung condition, the more so as this patient twice suffered from attacks of rheumatic fever (1926 and 1938). Rheumatic lung was defined by Hadfield (1938) as "a non-committal title for a highly characteristic variety of massive pulmonary consolidation which occasionally complicates rheumatic carditis in its acute infective phase". This definition certainly does not fit our case where neither a massive consolidation of the lungs nor an active carditis

1

2



3

4

- Fig 1—Nov 24 1943 Six months prior to onset of present illness the lungs are normal
 Fig 2—June 21 1944 Numerous opacities, especially in basal areas
 Fig 3—July 20, 1944 Miliary dissemination in both lungs
 Fig 4—August 13 1944 Ground glass appearance of both lungs

HEILIG-RHEUMATIC LUNG

THE INDIAN PHYSICIAN—Sept 1940

5

6



Fig 5—September 15 1944 Clearing of the upper lung fields.

Fig 6—October 5 1944 Only increased lung markings left

Fig 7—Feb 22 1945 Nine months after onset of illness six months after starting salicylate treatment the lungfields are clear except for peribronchial thickening of lower part of right hilum

7

was present, but in the light of more recent investigations a massive consolidation is not typical for rheumatic pneumonia. *Neuburger et al* (1944) summarise their experiences in eight cases of which they report clinical, radiological and post-mortem findings saying " roentgen changes with one exception (case 4) were not of specific diagnostic value. In case 4 the widely disseminated fine stippling and mottling resembled early miliary tuberculosis. Such a roentgen finding in association with the symptoms mentioned would suggest the clinical diagnosis of rheumatic pneumonia." These authors come to the conclusion that a radiological picture resembling miliary tuberculosis, such as was seen in our case, is diagnostic of rheumatic pneumonia because the specific lung lesions caused by rheumatic fever, consisting of specific granulomas, called "Masson bodies", of focal alveolitis with necrosis, hyaline lining membrane, etc., are decidedly discrete and usually not confluent, the "Masson bodies" do not even extend beyond a single alveole. Here it should be mentioned that *Epstein and Greenspan* (1941) recognize the histological findings in the lungs of rheumatic fever cases only as characteristic but not as specific.

The difficulty in identifying our case as one of rheumatic pneumonia mainly consists in the fact that in all such cases—in the literature available to us—rheumatic fever affected heart and lungs simultaneously, in the words of Hadfield (1c) "active carditis is an invariable accompaniment of these changes". And yet, it seems conceivable that our patient with the history of two previous rheumatic fever attacks which affected only his joints, this time suffered from an attack of rheumatic fever, characterised by a sedimentation rate of 60/100 mm, sweats, occasionally some slight pain in the knee, remittent fever which disappeared literally over night in response to salicylates and a rheumatic pneumonia which almost equally speedily improved on salicylate medication while his heart remained clinically unaffected. Unfortunately, we cannot definitely exclude a subclinical affection of the myocardium as an electrocardiogram was taken only in convalescence, though this was normal. But at no stage of this illness were there present any signs or symptoms of endocarditis, especially valvulitis. Neither were change of heart sounds nor a murmur, nor undue tachycardia, pain or palpitation ever noticed or complained of, radiologically, size and outlines of the heart remained constant. Therefore, it seems possible that under certain conditions, which apparently rarely materialise, rheumatic fever appears clinically, apart from fever, changes of morphological blood picture and increased sedimentation rate only as a rheumatic pneumonia.

The absence of a pronounced involvement of the joints during this attack is less surprising than the normal findings on the heart because the picture of a fully developed acute rheumatic polyarthritis is rarely seen in India although rheumatic heart disease is equally as common here as in Europe.

Another approach to the diagnosis of the cause under discussion, leading to similar conclusions, is based on investigations by *Rich and Gregory* (1943), they "have recently shown that cardiac

lesions, having the basic characteristics of those of rheumatic fever, can be produced experimentally as a reaction of anaphylactic hypersensitivity to foreign protein" The same authors made it probable that the pulmonary lesions of rheumatic fever equally are of anaphylactic origin

These remarkable results justify an attempt to classify our case as an allergic reaction to an unknown agent, a reaction such as rheumatic fever is All the syndromes which had to be considered here for the differential diagnosis very probably are of allergic origin and the constant, though moderate, eosinophilia of the reported case points in the same direction Leoffler (1c) suspected ascaris toxin as the responsible allergen in the condition named after him and recently an unusually well observed case (Sommer, 1943) proved that roundworms are capable of producing an eosinophilic pneumonia For tropical eosinophilia Heilig and Visweswar ('43), Patel (1943 1944, 1945), Menon (1945) and others made an allergic origin more probable than any other aetiological factor But the strongest argument for the possibility that allergic processes might cause pathological conditions similar to those described here is a clinical entity, called bagasse disease (Sodeman & Pullen, 1944) It is a pneumonitis, observed upto now in 18 cases, due to contact with bagasse, the product remaining after extraction of sugar from sugarcane Clinical picture, character of fever, white blood picture and, specially, the radiological lung condition (ground glass appearance) are identical with our case The only difference, though an essential one, is that all the people in whom bagasse disease was observed, professionally handled bales of sugarcane straw whereas our patient is a solicitor who, to his knowledge, never came near this material Thus, probable though the allergic nature, rheumatic or otherwise, of the reported case is, we were unable to determine the causative factor, the responsible allergen

Summary and conclusion A case is reported, presenting remittent fever of three months' duration, a slight leucocytosis with moderate eosinophilia and a radiological appearance of the lungs resembling miliary tuberculosis All the pathological signs and symptoms responded dramatically to salicylate medication It is discussed whether this pathological condition could have been one of rheumatic pneumonia, i.e. an attack of rheumatic fever, involving only the lungs Another eventuality is that this clinical picture was due to an allergic reaction of some other than rheumatic origin

My thanks are due to Dr J F Robinson M.D., F.A.C.S., F.R.C.S.E., Director of Medical Services, Jaipur State for valuable suggestions, to Dr Bhawanil Shankar M.B., B.S. our radiologist, and Dr Gulabchand Sharma, his assistant, for carefully taking and skilfully reproducing the skiagrams

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(Continued on p 223)

TIN IN TYPHOID FEVER

REPORT OF 50 CASES OF TYPHOID FEVER TREATED WITH ALDESTAN, AN ORGANIC TIN COMPOUND

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Following the report of Reitler and Marberg (1943) on the bactericidal effect of metallic tin on *E typhi*, and on the use by them of tin stearate and metallic tin in typhoid fever with favourable clinical results, it was decided to treat with their tin preparation (Aldestan), a series of cases of typhoid or paratyphoid fever admitted under my care in the K.E.M Hospital, and in the P G Singhane Hindu Hospital, Bombay Fifty* unselected serial patients suffering from clinical typhoid fever admitted under me in these hospitals from October 1945 to July 1946 were treated with the tin preparation, and fifty serial cases admitted in other wards during this period and treated in the orthodox fashion were taken as control The diagnosis of typhoid or paratyphoid fever was based on clinical evidence, positive widal reaction, and in some cases by the culture of *B typhosum* or *paratyphosum* A, or B from the blood Isolation of the organism from faeces or urine, or following up the carrier state, was not possible due to the lack of laboratory facilities In this report the clinical label typhoid fever will be used to include typhoid fever and paratyphoid fevers A or B caused by *E typhi*, *Salmonella paratyphi*, or *Salmonella Schottmulleri* respectively

ALDESTAN

The preparation used was a proprietary tablet, called *aldestan*, manufactured by Chemica Ltd., of Haifa, Palestine, for oral use and described by them as an organic tin compound, *Heptadecyl Aldehyde Stanoxystearate plus Stannum Colloidale*, each tablet containing 0.012 gram of metallic tin

Dosage For an adult 5 tablets per day were given for 12 days The tablets were thoroughly crushed and given in water or milk every 4 hours For children under the age of 10 years, half a tablet per each year of age per day was used To enhance the therapeutic action of the drug potassium iodide, 5 grains per ounce was given with each dose (i.e. 25 grains of potassium iodide per day) to the adults and a smaller dose in proportion to age was given to children, as recommended by the manufacturers All patients were given a diaphoretic mixture four hourly and after the seventh day a mixture containing 10 grains of sodium salicylate and 3 grains of acid acetylsalicylic thrice daily to counteract the rise in temperature due to the tin preparation. It appears that this antipyretic mixture is better given from the beginning throughout the course of

* Since writing this report I have treated 12 more cases of typhoid fever with aldestan, without any fatality, and without any new evidence to alter the conclusions arrived at in this paper

aldestan This course of 60 tablets was completed in all cases even if the temperature came down to normal earlier This was considered necessary because, on theoretical grounds if the drug was stopped early, there was a definite risk of relapse

Dietetic, symptomatic and nursing treatment was given to all patients on orthodox lines

Contra-indications There were no contra-indications to the use of the drug The drug was well-tolerated, though it showed a tendency to cause a slight rise in daily maximal temperature and some increase in the frequency of bowel movements in patients with diarrhoea But these were not indications for stopping the drug Likewise intestinal haemorrhage or a history of it was also not a reason for withholding the drug This complication is said to be less frequent and less severe, with its use *Sulphamylamides* are said to be toxic if administered by mouth together with aldestan They are said to be perfectly well-tolerated if given by injection Where sulpha drugs are indicated for secondary infections the manufacturers recommended that these should be given by injections, or if oral administration is desired, aldestan should be stopped for 12 to 24 hours before starting the sulpha drugs *Penicillin* was used for secondary infections in this series of cases, where penicillin was not available, the above advice was followed

Tolerance and toxic manifestations The drug was well-tolerated by all patients There were no gastric symptoms, except negligible nausea in a few patients There were no toxic manifestations which could be attributed to aldestan except, (1) slight increase in daily maximal temperature, (2) some increase in the frequency of bowel movements, (3) a fall in leucocyte count in 2 cases, and (4) an increase in temperature, mental confusion, and toxic state in 2 cases The first two disturbances were of little consequence and could easily be controlled by antipyretic and astringent drugs

In all cases the total blood count was done before starting the treatment, and later, the white and differential cell count every two days In *two* cases (4 per cent) the *white blood count* fell to 1500 and 1300 per cmm after 20 to 30 tablets were given and the drug had to be stopped These were not cases of agranulocytosis because though there was a proportionate reduction in the granulocytes they never became too low or disappeared completely, nor was there any sepsis in the mouth or throat Within a week after withdrawing the drug the count rose to or above 5000 per cmm without any special treatment In other cases the leucopenia due to typhoid infection disappeared and the count steadily rose to 5500-7500 per cmm There was no significant change in the red blood cell count or in the haemoglobin percentage

In *two* cases (4 per cent) the *mental condition* deteriorated Torpor, confusion, and restlessness increased together with rise in temperature and in pulse rate, and the patients appeared more toxic On withdrawing the drug the patients returned to their previous state After five days, the drug was started again with a

similar result suggesting the action of the drug on the nervous system. In one patient after 10 days' withdrawal the drug was started a third time with the production of the same clinical picture. There was no change in the white blood count in both of these patients and the toxic effect was probably due to the direct action on the central nervous system. The cerebral symptoms though alarming disappeared entirely on the withdrawal of the drug.

RESULTS

Mortality In this series of 50 cases only 4 died (8 per cent) while in the control cases 12 died (24 per cent) (see Table). The

TABLE

	Aldestan treated 50 cases		Control 50 cases	
Mortality	4 (8%)		12 (24%)	
	Haemorrhage	2 (4%)	2	(4%)
	Perforation	1 (2%)	1	(2%)
	Toxaemia	1 (2%)	8	(16%)
	Pulm Embolism		1	(2%)
Toxic symptoms	Leucopenia	2 (4%)		
	Encephalopathy	2 (4%)		
Fever	Average Number of days of duration of fever in 46 cases — 29 days			
	Favourable Response	37 (84%)		
	Favourable Response with Relapse	5 (10%)		
	Incomplete Response	5 (10%)		
	No Response	8 (16%)		

deaths were due to haemorrhage 2, perforation 1, and toxaemia 1, in the control group the deaths were due to haemorrhage 2, perforation 1, and toxaemia 9. Thus there was a marked reduction (by 66.6 per cent) in the mortality rate. Deaths from the complications, haemorrhage and perforation, were the same in both groups, the reduction was in deaths from toxaemia or vascular atony or peripheral failure. The clinical impression that aldestan reduces the absorption of toxins is strengthened by this comparison of mortality rates.

Toxaemia Of the 50 cases, 46 cases showed a definite improvement in the general clinical condition. The toxaemia was much less and patients required little attention. The ward sisters and housemen all agreed that the aldestan-treated patients required very little special attention, even when the temperature showed

no signs of settling. This improvement in the clinical condition became apparent in the first 5 days. Even the most severely toxic patients showed a remarkable change in the clinical condition after 3 to 5 days i.e. after 15 to 25 tablets were administered. The two cases in which the mental confusion increased, the deterioration occurred during this period, so it can be said that the patients who tolerate 15 to 25 tablets are not likely to have any cerebral symptoms later on. The two cases where there was progressive leucopenia, showed this abnormality also in the first 5 days. In these patients there was no deterioration in the toxic state, on the contrary the general clinical condition was the same, or a little better. Leucopenia was merely a routine laboratory finding, which disappeared on stopping the drug.

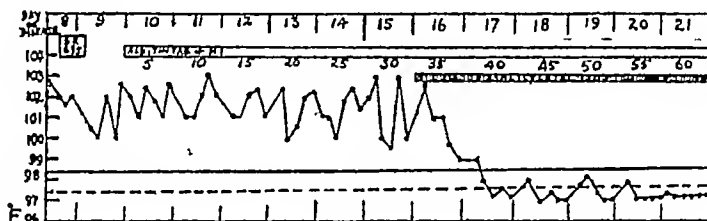


Chart 1

FEVER

Duration of febrile state. On the average the total duration of fever is not appreciably reduced. Leaving out the four cases that died, the average duration of fever in 46 cases was 29 days, this is about the same as in the control group. The average duration of fever, in cases that responded favourably, counting from the first day of aldestan treatment, was about 10 days (the shortest duration being 3 days and the longest 17 days).

Favourable response. The drug was given for 12 days. After about 25 to 35 tablets were given, the temperature curve showed a

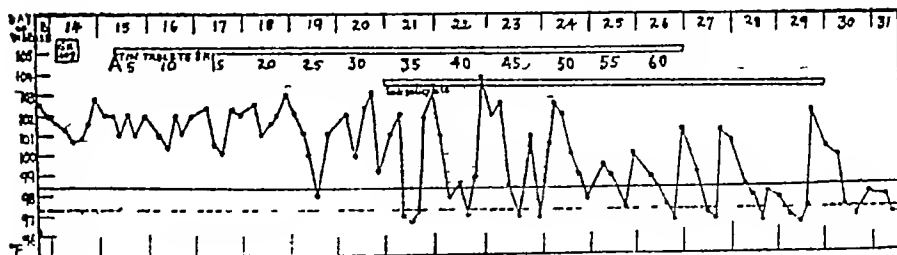


Chart 2

change. The daily maximal rise increased a little, and at the same time the daily minimal temperature also fell. In some cases this continued for 3 to 4 days before the temperature reached normal.

and remained so (chart 1), in others this swing persisted throughout the course of aldestan, the temperature disappearing in 3 to 5 days after stopping the drug (chart 2) In this series the fever came down to normal and remained so before the course was over in 12 cases In 20 other cases the fever came down within 3 to 5 days after stopping the drug Thus there was a favourable response in 32 cases (64 per cent)

Favourable response with Relapse 5 cases with a favourable response had a relapse within 10-14 days after stopping the drug A second short course of 30 to 40 tablets of aldestan always brought down the temperature in 8 to 10 days

Incomplete response When the fever did not come down within 5 to 10 days after stopping the drug, though the temperature curve showed an altered range, the case was considered to be one of incomplete response There were 5 such cases in this series In these cases a second course of aldestan for 8 to 12 days (40 to 60 tablets) produced a satisfactory defervescence (chart 3)

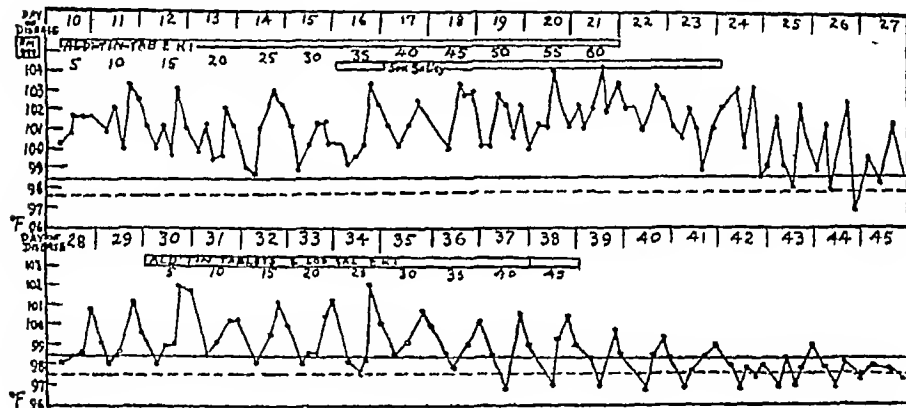


Chart 3

No response There were 8 cases where the drug apparently failed to produce any effect on the temperature curve

DISCUSSION

There is no specific treatment in typhoid fever, except Felix's antityphoid serum and bacteriophage. Both these rational measures are practically unavailable in Bombay. Non-specific treatment, with vaccines or heavy metals have been used from time to time, sometimes with good, sometimes with disastrous results. The writer had used bismuth in the form of iodobismuthate of quinine, 0.1 gm in 3 cc every 4th day, in some 30 cases in 1932-33, and had found it useful in controlling the toxæmia and fever, but was obliged to discontinue its use because of the heavy incidence of stomatitis.

Tin has been used for a long time by Ayurvedic physicians in fevers of long duration and in many other conditions in the form

of वगभस्म Its use against staphylococcal infections of the skin is popular with clinicians Reittler and Marberg have produced experimental evidence that tin has bactericidal effect against *E. typhi*, *Salm paraty A & B*, *P. pestis*, *Staphylococcus aureus*, *B. dysent flexner*, *Esch coli*, and *Bruc melitensis* Marberger and Zipser have noted that when dogs are given organic tin by mouth for 15 to 30 days they do not show any toxic manifestations, and on post mortem, they show a considerable enlargement of *Peyer's patches*, the *mesenteric lymph nodes*, and the *intestinal mucous membrane* due to the deposition of the metal in these tissues It is also deposited to a lesser extent in the *bones*, *skin*, *muscles* and the *liver* The elimination is slow, via the faeces and to a lesser degree through the urine In view of the experimental evidence it is reasonable to expect that the presence of tin in these areas for a long time will have a bactericidal or sterilising effect on the typhoid organisms which thrive in these lymphoid areas The clinical evidence appears to support this belief

Typhoid organisms are not susceptible to sulphonamides, or to penicillin in the usual sense of the term Bigger has produced laboratory evidence that the growth of the organism can be retarded in the presence of high concentrations of sulphathiazole and penicillin He has suggested, on laboratory evidence, the use of large doses of sulphathiazole and penicillin for 8 days in clinical typhoid, to produce a high concentration in the blood of both these drugs for a definite period McSweeney has reported 5 cases treated on Bigger's suggestion The first case was given doses of penicillin appropriate for a staphylococcal infection, with no appreciable effect on the pyrexia or blood-cultures, although toxæmia was much lessened, and there were no complications due to ulceration The next four cases were treated intensively with penicillin and sulphathiazole, receiving two courses, each of 4 days with a 4 days interval, and each comprising of 10,000,000 units of penicillin (200,000 units i.m./2 hrly) and 34 g of sulphathiazole (2 g i.v. and 1 g/3 hrly by mouth) given in four days Speedy disappearance of toxæmia, subsidence of pyrexia, and disappearance of organisms from the blood, faeces, and urine followed the end of the second course in three of the four cases In the fourth case, when the second course was postponed for about a fortnight, there was a relapse, which rapidly subsided when the second course was initiated Most clinicians will hesitate to use such large doses of a toxic sulpha drug and troublesome and expensive 20 million units of penicillin It will be advisable to see experimentally and clinically if typhoid organisms appear more vulnerable to a combination of tin and penicillin or tin and Felix's anti-typhoid serum or a combination of all three

SUMMARY AND CONCLUSIONS

1 Fifty cases of typhoid fever were treated with an organic tin compound,—aldestan

2 The drug was found to be perfectly safe and well-tolerated, the only serious toxic manifestations observed being leucopenia (4 per cent) and mental confusion (4 per cent),

3 The clinical results were favourable in reducing the mortality rate (by 66·6 per cent) and in greatly diminishing the toxæmia, the subjective improvement being very marked in all cases

4 The fever came down by lysis in 3 to 17 days after starting the drug. The average length of febrile period was not much affected

5 It is not possible to say whether tin acts directly on the bacilli or indirectly through stimulating the reticuloendothelial system

6 In this study it was not possible to observe the effect of the drug on the complications or on the carrier state

7 It will be interesting to watch the effect of the drug used as early as possible, and with penicillin or with Felix's anti-typhoid serum or with both

8 In the absence of any specific therapy available at present, tin appears to be the drug of choice in the treatment of typhoid—paratyphoid fevers

I should like to thank Major Surjan Singh of Lahore for a liberal supply of aldexan for clinical trial, my successive house physicians Drs. Shroff and Bhatt and Ward Sister Gamir of the K. E. M. Hospital and Drs. Wani and Bhadri and Sister Wray of the P. G. S. Hindu Hospital for personally supervising the treatment and making the duplicate charts for me and Dr. Munshi Medical Registrar K. E. M. Hospital, for help in analysing the case records, and the heads of both these hospitals

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| REITLER R. AND MARBERG K. (1943) | The Bactericidal Effect of Tin and its Application to the Treatment of Typhoid Fever
<i>Trans. R. S. Trop. Med. & Hyg.</i> 38 5, 305
March |

CIRCULATORY FAILURE AND ITS TREATMENT

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(Continued from page 159)

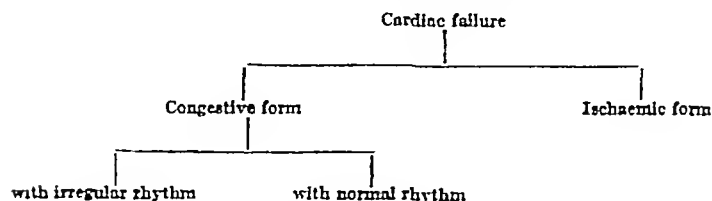
CARDIAC FAILURE

In order to understand our present day conception of cardiac failure it is necessary to have an idea of what is meant by the cardiac reserve or reserve power of the heart, these terms denote the power of accommodation of the heart to the various stresses and strains of life, a sort of safety valve that comes into operation whenever the body, by indulging in excesses of any kind, tends to overwhelm the heart. It is said that during spells of intense muscular activity, the cardiac output in a trained athlete may increase to even 900 per cent of the basal value (Fishburg), which fact gives us some idea of the enormous reserve power of the heart. The reserve power of the heart is not a fixed quantity, it is a variable factor influenced by rest, training, etc. With failure of the heart, there is a curtailment of this reserve power, if the latter disappears completely, signs of failure will be apparent even at rest, under basal conditions.

The term cardiac failure has been defined differently by different authors. Crichton Bramwell defines it as "an inability on the part of the heart to maintain an output of blood adequate to meet the requirements of the body". Beckman defines heart failure as "the state of broken compensation in which the heart is no longer able to perform the amount of work necessary if the body as a whole is to maintain a condition of normal activity". Fishburg, who regards the condition from a clinician's standpoint, defines it as a "limitation of the activities of the patient which symptoms or signs reveal to be engendered by defective circulation of the blood". From a practical point of view, a convenient definition of cardiac failure would be A limitation or curtailment of cardiac reserve (or reserve power of the heart) resulting in an inability on the part of the heart to cope with the demands imposed upon it by the body.

Many different classifications for cardiac failure have been suggested, most of them being rejected later on the grounds of being inaccurate or inadequate. A classification of cardiac failure into acute and chronic, serves no useful purpose, there being no hard and fast line of demarcation between these forms.

There is a tendency on the part of the British cardiologists to consider cardiac failure under two headings

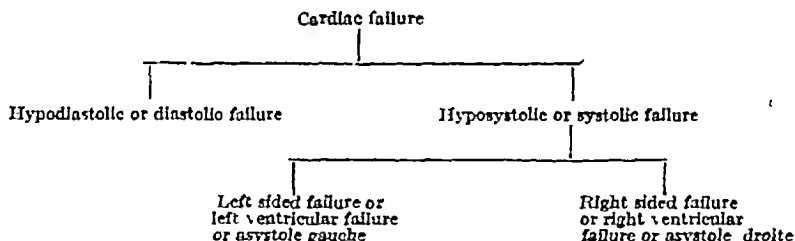


The initial symptom in congestive cardiac failure is shortness of breath or dyspnoea whilst in the case of the ischaemic form it is cardiac or anginal pain. This classification serves to distinguish

types of failure with normal from those with abnormal rhythms, an important distinction from the point of view of prognosis and treatment. According to Bramwell, in the congestive form of failure, the output of the heart is inadequate for the requirements of the whole body, while in the ischaemic form the deficiency usually affects an isolated group of muscles only. The above classification is far from perfect. It fails to recognize systemic and pulmonary congestion as distinct entities, a distinction of utmost value in practice. Except for a cursory division of the congestive form into the "type with normal" and "the type with abnormal rhythms" no attempt has been made to recognize individual circulatory syndromes, they are indiscriminately grouped together under the generic term of congestive cardiac failure, in spite of their having recognisable characteristics.

A more useful classification has recently been evolved on the European continent, and in America, this new conception of cardiac failure owes its origin to French clinicians.

The heart fails to discharge its functions adequately when either systole or diastole (the two phases of the cardiac cycle) is deranged. "Hyposystolic failure" connotes a deficient "emptying" of the heart during systole. In "hypodiastolic failure", on the other hand, the defect lies in the diastolic filling of the heart and not its emptying. It is important to realize that there is no actual "sucking in" of blood into the heart during diastole, when the heart muscle relaxes,



blood flows in passively into the heart-chambers. The heart subserves the function of a force-pump to the circulation, not that of a suction-pump. There is a tendency on the part of some cardiologists to regard diastolic failure of the heart and peripheral failure as identical (Bramwell), it is true that diastolic filling of the heart in peripheral failure is deficient, but that is no justification for regarding the two conditions as identical. The initial defect in peripheral failure lies in the peripheral circulation while in the case of diastolic failure the defect is primarily cardiac and not peripheral.

Hypo-Diastolic Failure

This type of cardiac failure, which is much less frequent than the hyposystolic variety, occurs in two main groups of conditions.

(1) During paroxysms of high-grade tachycardia. During bouts of tachycardia or auricular fibrillation or flutter, the ventricular rate may attain values of 200 or more, as a result, the duration of the cardiac cycle is reduced, usually at the expense of the diastolic phase, the "rest phase" of the heart. When the diastolic filling of the heart becomes inadequate from the shortening of the d

symptoms and signs of diastolic failure of the heart make their appearance

(2) In pericardial diseases like pericardial effusion and chronic constrictive pericarditis. In cases of so-called cardiac tamponade, collections of fluid within the pericardial sac or fibrous thickening of the pericardium (as the case may be) limit the normal expansion of the heart during diastole, as a result, diastolic filling of the heart becomes deficient and heart failure ensues

Whereas tachycardia induces diastolic failure by shortening or limiting the period of diastole, pericardial disease induces it by limiting the expansion of heart chambers during diastole

Hyposystolic Cardiac Failure

Hyposystolic cardiac failure has been subdivided by French clinicians into two distinct syndromes, depending on whether the left ventricle or the right ventricle fails first

(1) Left sided failure or left ventricular failure or "asystole gauche"

(2) Right sided failure or right ventricular failure or "asystole droite"

Left-Ventricular Failure

Primary insufficiency of the left ventricle of the heart perhaps constitutes the commonest form of circulatory failure encountered in practice. Attempts to subdivide left sided failure into "left auricular failure" and "left ventricular failure" are futile and serve no useful purpose since the alteration in circulatory physio-dynamics is similar in the two cases

Important causes of left ventricular failure are

(1) Hypertension, essential or renal. The left ventricle, which has to work against resistance, is overworked and tends to give way

(2) Diseases of the aorta, e.g. aortic regurgitation and aortic stenosis

(3) Coronary artery disease. Thrombosis or obliterative disease of the left coronary artery or its descending branch results in a diminished blood supply to the left ventricular musculature with corresponding weakness of its contractile elements

(4) Mitral regurgitation. In this variety of valvular disease, the regurgitated volume of blood during ventricular systole is added to the blood entering the left auricle from the pulmonary veins, as a result, the left auricle holds an extra large amount of blood, during diastolic filling of the left ventricle, the opening of the mitral valve allows this large amount of blood in the left auricle to flow into the left ventricle and increase its diastolic volume. In accordance with Starling's law of the heart, such stretching of muscle fibres (of the left ventricle) during diastole leads to increased systolic discharge. The net result is that in this disease of the valve, the left ventricle is subjected to excessive strain and tends to fail

In stenosis of the mitral valve, the maximum strain falls on the left auricle after which it falls on the right and not on the left ventricle

Clinical picture The clinical manifestations of left ventricular failure are easy to understand if we remember the basic fact that in this type of failure there is a pulmonary engorgement without systematic venous engorgement. Main features are

(1) Dyspnoea or shortness of breath is the earliest and the most striking of the symptoms. The dyspnoea may occur after physical effort (exertional dyspnoea), occur spontaneously or at rest (paroxysmal dyspnoea or cardiac asthma) or be continuous (continuous dyspnoea). The patient frequently adopts a sitting-up posture in order to relieve the dyspnoea (orthopnoea).

While in left-sided failure of the heart, dyspnoea is much more noticeable than cyanosis, the reverse often holds good in cases of right sided failure.

Amelioration of dyspnoea or of other symptoms of pulmonary engorgement in cases of left ventricular failure does not necessarily mean clinical improvement or response to therapeutics, not infrequently, such apparent amelioration of symptoms heralds the onset of right ventricular failure. Right ventricular failure, when superimposed on left-sided failure, tends to lessen rather than increase the previous disability or distress.

(2) Cough, with or without expectoration. In individuals of advanced years, cough may be the first or only symptom of an insidious cardiac insufficiency. A rusty brown-coloured sputum is common in such cases, microscopic study of such a sputum reveals the presence of so-called "heart failure cells" (Herzfehlerzellen of the Germans). Hoarseness of voice may arise in rare cases from pressure on the left recurrent laryngeal nerve by the engorged left pulmonary artery.

(3) Symptoms indicative of cerebral anaemia, such as vertigo, faintness and syncope are occasionally encountered in cases of left-sided failure, when diminished cardiac output leads to fall of arterial blood pressure, in most cases, such a fall of pressure is prevented by the compensatory mechanism of peripheral vasoconstriction. In aortic regurgitation symptoms of cerebral anaemia present themselves long before the onset of left-sided failure.

(4) Pulsus alternans. This sign of "myocardial fatigue" or "myocardial exhaustion" is by no means rare when searched for, especially by the sphygmometric method. When the pressure in the blood pressure cuff is gradually released after being raised to above the systolic pressure, an interesting phenomenon is observed. A sudden "doubling of sounds" is characteristic of pulsus alternans. To cite an actual case, 38 arterial sounds were heard from a pressure level of about 160 to about 154 mm Hg, on releasing more air from the cuff, a sudden doubling of the rate to 76 per minute was observed. "Electrical alternation" where deflections (especially the R waves) of the electrocardiogram show alternation in amplitude, is a very rare phenomenon indeed. I have observed it on three occasions only. In one case, alteration of R waves was only obvious during a paroxysm of auricular flutter.

(5) Gallop rhythm or bruit de gallop or reduplication of the first heart sound of a characteristic type is a common manifestation

of left sided failure, it is best heard just internal to the apex-beat. Bramwell lays stress on the even spacing of the three sounds in such cases. Two other features of true gallop-rhythm, which may be of value in difficult cases, are (1) The repudiation of the first sound is not only audible but also palpable. (2) Of the three sounds heard during each cardiac cycle, the loudest is the second.

(6) Oedema is absent in cases of isolated left sided failure, according to most present day authorities. Though this rule may hold good for the great majority of such cases, it is nevertheless open to exception. Cases of left ventricular failure with persistent oedema or 'puffiness' of the ankles are occasionally encountered. In the complete absence of all other signs of right sided failure, there is no venous engorgement or pulsation, the liver is not congested or enlarged, there is no cyanosis, no ascitis and no hydrothorax, the venous pressure is normal and yet there is persistent oedema of the ankles. To explain such oedema on the basis of an early right sided failure appears illogical since it may continue for a considerable time without any other sign of right sided failure appearing. The oedema in such cases is difficult to explain. It may be due to lack of oxygen to the peripheral tissues and capillaries, partly due to an impaired systolic output from the insufficient and weakened left ventricle and partly from deficient oxygenation of blood in the lungs, which are chronically engorged, lack of nutrition to the peripheral capillaries would increase their permeability to protein etc, with resultant oedema.

(7) Absence of hepatomegaly and lack of venous engorgement. In occasional cases of left-sided failure, there is a raised venous pressure, the raised pressure in such cases has been fully explained by Fishburg in his monumental treatise on Heart Failure.

(8) Physical examination of the lungs usually reveals

(a) Presence of crepitations, mostly basal. I have found such crepitations to be both more common and more profuse on the left side of the chest.

(b) Presence of a "functional emphysema". Because of the engorged state of the pulmonary vessels, normal relaxation of lung-tissue during expiration fails to occur, as a result, the lungs maintain a position of partial inspiration or distension, even during the expiratory phase.

Special Investigations

(1) The radiological appearance of the chest in cases of left sided failure is very interesting. The radiological picture of pulmonary hyperaemia is both varied and interesting.

(2) Circulation time. There is a characteristic prolongation of the arm-to-tongue circulation time with a normal arm-to-lung circulation time in cases of pure left ventricular failure, at least in the early stages. Circulation times were investigated by me in ten cases of isolated left ventricular failure associated with hypertension. The methods of determination employed were the Calcium gluconate and the Magnesium sulphate methods for the arm-to-tongue time and the "ether method" for the arm-to-lung time. The Magnesium sulphate method of determining the arm-to-tongue time was found to

be the most convenient of all the methods advocated for this purpose. The end-point is quite sharp and easily detected, the cost of the solution is negligible and there are no toxic side-effects. In the opinion of Bernstein and Simkins, Magnesium sulphate fulfils the criteria for the ideal circulation-time agent. The arm-to-tongue time (measured by the magnesium sulphate method) measures the "circulation as a whole" and varies from about 8 to 18 secs, with an average of 13.5 secs, in normal subjects. With this method, the circulation time, in twenty cases of isolated left-sided failure investigated, ranged from 12 to 22 secs, with an average of 16.6 secs. The Calcium gluconate method which was abandoned after a fair trial gave higher figures in the great majority of cases. The technique employed for the Magnesium sulphate method was simple. 7 ccs of 10 per cent magnesium sulphate solution were rapidly injected into one of the anti-cubital veins, the end-point was indicated by a feeling of intense heat in the pharynx.

The "ether time" or the arm-to-lung time was also determined in these cases. It gives a "rough measure of the functional capacity of the right ventricle". The ether time in these cases ranged from 5.8 to 10.6 secs with an average of 7.7 secs. 5 minims of ether and 5 minims of normal saline are injected intravenously into one of the arm veins in order to determine the arm-to-lung time. Normal ether time varies from about 3.5 to 8.0 secs (Hitzig).

The "lung-to-tongue time" was calculated in these cases by subtracting the "ether time" from the "Magnesium sulphate time". The actual figures in these cases varied from 7 to 12 secs with an average of 9.7 secs. Hitzig determined the normal, "saccharin time-ether time difference", which serves as an index of the functional capacity of "the left heart unit", in 52 normal subjects, he gives the range as 4.5 to 9.5 secs. The "lung-to-tongue time" is a very useful figure, giving a "measure of the functional capacity of the left ventricle".

(3) The venous pressure usually remains unaffected in cases of left-sided failure of the heart. Venous pressures were determined in the aforementioned cases of left ventricular failure, with the B.D. Venous Pressure Apparatus. Figures ranged from 60 to 23.4 cms of water in these cases with an average of 11.0 cms. High levels were reached in only two cases, the venous pressures being 23.4 and 20.0 cms of water. Excluding these two cases, which are probably associated with "incipient right ventricular weakness", the average value for venous pressure was 8.5 cms of water.

(4) The vital capacity of the chest is said to be diminished in cases of left-sided failure.

Pulmonary Oedema or Oedema of the Lungs

The exudative form of pulmonary congestion, where the patient coughs up pints of pink frothy sputum, displays a highly characteristic clinical picture. Fortunately infrequent, acute pulmonary oedema is dramatic in its onset and leaves an indelible impression on the mind of the observer. Attacks are usually observed in elderly hypertensives, especially in subjects of cardio-renal disease. Attacks may follow some mild exertion, emotional outburst or respiratory infection. A hypertensive, aged 93, developed acute pulmonary

cedema a couple of hours after indulging in the effort of attending a tea-party! In many cases, attacks of pulmonary oedema arise spontaneously

More common, to my mind, than acute pulmonary oedema is a symptom-complex or syndrome which can perhaps best be described as a *subacute or chronic form of pulmonary oedema*. There is no mention of this syndrome in the text-books of medicine, as a result, the majority of clinicians are unaware of its existence. It seems to occur most frequently in elderly hypertensives, in whom it constitutes one form of "cardiac death". After observing a fair number of such cases, I am able to give the following description of the syndrome—The patient is usually a middle-aged or elderly hypertensive (or sometimes a case of aortic regurgitation) who has had a mild degree of pulmonary congestion for a considerable time, often for years. There have been crepitations at one or both lung-bases, with or without "prolonged expiration". Curiously enough, basal crepitations in hypertensives seem to occur more frequently on the left side than on the right, unlike pleural transudate, (or hydrothorax) which shows a predilection for the right side of the chest. It is possible that the large **ventricular mass** on the left side of the chest in cases of hypertension or aortic regurgitation may be responsible for the frequency of crepitations on the left side, the ventricular mass may be engendering a state of partial lung collapse on the left side.

After a variable period of time, varying from a few months to several years, the crepitations spread to the entire extent of both lungs, even within the space of a few hours. The factor responsible for such a spread is in most cases a respiratory infection like influenza, bronchitis or common cold, in other cases, it is preceded by an attack of anginal pain, which may be of the nature of "acute coronary insufficiency" described by Levy and Bruenn and attributed by these authors to blockage of a small coronary twig or branch. With the generalization of the crepitations, the patient becomes dyspnoeic and unable to assume the recumbent posture. Unlike acute pulmonary oedema, there is no oozing-out of large amounts of pink and frothy sputum, instead, there may be small amounts of muco-purulent expectoration with the cough, a constant feature of the syndrome. There is a steady fall of arterial blood pressure, the systolic pressure, which appears to bear the greater brunt and starts falling first, may attain very low figures, e.g. 60 mm of Hg. An interesting auscultatory phenomenon, I have observed almost consistently in these cases while taking their arterial pressures, is a disappearance of the normal thudding sounds with the result that the entire duration of the differential or pulse pressure is taken up by a murmurish sound. The extremities are usually cold and clammy, there is no increase of peripheral oedema, chest pain is not encountered in these cases. The veins are sometimes engorged and may be pulsating, the venous pressure was determined in two such cases, in both, high figures were obtained, viz, 23.8 and 27.0 cms, venesection gave temporary amelioration of symptoms in both cases. The pulse is unusually rapid (100 to 150 per minute) and of

low volume There is no rise of temperature throughout the attack The leucocyte count has not been investigated in these cases Electrocardiograms are not distinctive at any stage, the only characteristic common to all electrocardiograms is a low voltage, the maximum deflection in the electrocardiogram measures less than 5 mms One of my cases developed auricular fibrillation during the attack Sharply inverted and spiked T waves, deflected ST periods and prominent Q waves, such as are encountered in cases of coronary thrombosis, are not seen

After a few hours or days, the patient who has been getting progressively more dyspnoeic and depressed, expires quite suddenly for no apparent reason.

The clinical picture described above recalls that of the "dyspnoeic form of coronary thrombosis", where pain in the chest is absent The following features assist us in excluding coronary thrombosis

- 1 Complete absence of pain in the chest
- 2 Electrocardiographic alterations typical of coronary occlusion fail to appear Low voltage curves and flat T waves are the sole abnormalities encountered
- 3 Maintenance of a normal body temperature

(To be continued)

(Continued from p 208)

PATEL, N D	Allergic bronchitis with eosinophilia	Indian Physician	2	333	(Sept) 1943
id	Pulmonary hypertension	ibid	3	9	(Jan) 1944
id.	Benign eosinophilia	ibid	4	93	(May) 1945
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SODEMAN, W A & PULLEN R L	Bagasse disease of the lungs	Arch, Int Med	73	365	(May) 1944
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WEINGARTEN, R J	Tropical eosinophilia	Lancet	1	103	(Jan 23) 1943

CORRECTIONS —

Please make the following corrections in the article on Rheumatic Heart Disease by T K. Raman and P Ramkrishna Mudaliar, Indian Physician, V-8 177-186 (Aug) 1946

- (1) On page 177, instead of K T Raman, read T K Raman
- (2) Plate II instead of Fig 9, read Fig 10, and instead of Fig 10, read Fig 9
- (3) On page 184, in the last 3 lines of paragraph 3, delete 'S positive in Leads II, III, negative in Lead IV' and instead of 'S positive' read 'R positive' in Leads II, III

Critical Notes and Abstracts

THE EYE IN NUTRITIONAL DISEASE.—Ocular lesions may be the first sign of systematic disease, generalized infection, metabolic disturbances or nutritional deficiencies, in some disorders, such as arteriosclerosis lesions of the eyes may be the only sign to suggest the diagnosis. Thus, in the absence of other clinical signs and symptoms, examination of the eyes may reveal the only suggestion of latent nutritional inadequacy.

In a group of military personnel patients with faulty food intake, A. A. Knapp (Bull. New York Acad. Med. 22: 217, 1946) observed axial myopia, vernal catarrh (allergic conjunctivitis), hazy fundus oculi, chorioretinitis and optic nerve disease. Except for chorioretinitis each of these conditions had previously been shown to be associated with nutritional inadequacy.

Poor eyesight was the major complaint in Knapp's series of patients. Visual acuity of some eyes was 6/20 or even 5/20 with the other eye reading 8/20 or 12/20. Minimum reading of 15/20 in each eye had been required at the time of their enlistment. After administration of vitamin D and calcium for an unspecified period of time, over 50 per cent of those patients with progressive myopia showed either arrest or reduction of the condition. Approximately 33 per cent had less myopia; in some cases actual shrinkage of the myopic eyeball took place. A moderate percentage of myopic persons also have night blindness. The indicated therapy for myopia, suggests the author, may improve poor night sight.

Examination of patients who sought relief for 'inflamed' eyes accompanied by itching and photophobia, disclosed signs of vernal catarrh. Diagnosis of vernal catarrh was never made, however, without evidence of the pathognomonic stringy discharge. Since vernal catarrh is often asymptomatic, the condition may or may not have been present before onset of malnutrition. Vernal catarrh, like myopia and night blindness, was improved by vitamin D and calcium therapy.

Hazy fundus oculi and pallor of the optic disk have been observed in animals on depleted diets and may be a manifestation of latent nutritional disease. Several patients in this series had slightly hazy ocular fundi. Further examination revealed mildly blurred optic disk margins, there were 10 instances of thin peripheral rim of pallor, though rarely with diffuse pale pink color. Although physiologic blind spots, central form, and vision in many of these patients were normal, optic nerves of patients showing hazy ocular fundi and pallor of the optic disk cannot be considered healthy. The ocular fundi of these patients in no way resembled those of the civilian populations enjoying adequate nutrition.

Some patients with *pallor of the optic nerve* had enlarged blind spots. They almost always showed signs of malaria or focus of infection or both during the period of subnutrition. Except where retrobulbar retinitis accompanied multiple sclerosis, specific

treatment of the underlying infection cured the eye condition. Complete recovery usually followed elimination of foci of infection, use of other corrective measures and the intake of highly nutritious food.

Characteristic *chorioretinitis* was found in only a few patients, since the inflammation had not given rise to subjective symptoms. These patients improved within a few days with only dietary treatment consisting of ample intake of milk, fruits, meats, and vegetables, sometimes fortified with multiple vitamin supplement. An improved diet, without medication, also benefited patients with the more rarely encountered *chorioretinitis juxtapapillaris*.

In all diets, particular attention was paid to intake of calcium and vitamin D. Lack of these nutrients, points out Knapp, may be a potent cause of eye disease. Comparatively high doses of vitamin D were prescribed for all patients with progressing axial myopia, vernal catarrh, and night blindness.

Book Reviews and Notices

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY by Hamilton Bailey F.R.C.S. 10th Edn 1946. Published by John Wright & Sons Ltd., Bristol. Pp 876. Price 30 Shillings.

Hamilton Bailey, a practising Surgeon without an official teaching appointment, conceived of this illustrated manual of physical signs in clinical surgery for junior students as a holiday from his routine work. How well he has succeeded in his happy hobby is borne out by the fact that the book which appeared first in 1927 had in less than twenty years ten editions and seven reprints and also the good fortune of being translated in German and Turkish and whose Spanish, Portuguese, Italian, Greek and Dutch translations are at present in active preparation! This wide-spread popularity should be a sufficient guarantee of its worth.

Whether clinical surgery or medicine can be taught by written word only, however profusely illustrated with modern colouring and technique, we leave the clinical teachers and students to decide. A practical art can best be acquired by active apprenticeship to a craftsman, by diligent observation and imitation. No book can replace the out-patient teacher, no illustration can take the place of a patient. Yet, Bailey's book has earned its place in clinical teaching, by its clear-cut accurate descriptions, stimulating illustrations and historical allusions, which, if the student reads with Bailey and Bishop's *Names in Medicine and Surgery* will form a sound foundation for further clinical work. Medical education is really an acquirement of a method, and the student who follows Bailey has, we have no doubt, a reliable guide.

Reflections and Aphorisms

Research is fundamentally a state of mind involving continual re-examination of the doctrines and axioms upon which current thought and action are based. It is therefore critical of existing practices. Research is not necessarily confined to the laboratory.

although it is usually associated with an elaborate technique and complex instruments and apparatus which require a laboratory housing. This is controlled research which endeavours to pick out of the web of nature's activities some single strand and trace it towards its origin and its terminus and determine its relation to other strands. The older type of research involving observation and study of the entire fabric of disease largely with the help of the unaided senses, such as was the practice of doctors a century ago, has had its day, but backed by experience and a keen observant mind it even now occasionally triumphs over the narrow controlled research of the laboratory. It is the kind used by Darwin and other early biologists in establishing on a broad, comparative basis, the evolution of plant and animal life.

THEOBALD SMITH

Fear The mind delights in a static environment, and if there is any change to be itself the source of it. Change from without, interfering as it must with the sovereignty of the individual, seems in its very essence to be repulsive and an object of fear. A little self-examination tells us pretty easily how deeply rooted in the mind is the fear of the new, and how simple it is when fear is afoot to block the path of the new idea by unbelief and call it scepticism, and by misunderstanding and call it suspended judgment. The only way to the serene sanity which is the scientific mind—but how difficult consistently to follow—is to give to every fresh idea its one intense moment of cool but imaginative attention before venturing to mark it for rejection or suspense, as alas nine times out of ten we must do. In this traffic it is above all necessary not to be heavy-handed with ideas. It is the function of notions in science to be useful, to be interesting to be verifiable and to acquire value from any one of these qualities. Scientific notions have little to gain as science from being forced into relation with that formidable abstraction "general truth". Any such relation is only too apt to discourage the getting rid of the superseded and the absorption of the new which make up the very metabolism of the mind.

WILFRED TROTTER

Ideas It is a mistake to suppose, as it is so easy to do, that science enjoins upon us the view that any given idea is true or false and there is an end of it, an idea may be neither demonstrably true nor false and yet be useful, interesting, and good exercise. Again, it is poverty rather than fertility of ideas that causes them to be used as a substitute for experiment, to be fought for with prejudice or decried with passion. When ideas are freely current they keep science fresh and living and are in no danger of ceasing to be the nimble and trusty servants of truth. We may perhaps allow ourselves to say that the body of science gets from the steady work of experiment and observation its proteins, its carbohydrates, and sometimes too profusely—its fats, but that without its due modicum of the vitamin of ideas the whole organism is apt to become stunted and deformed and above all to lose its resistance to the infection of orthodoxy.

WILFRED TROTTER

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Original Contributions

PORTAL CIRRHOSIS

FURTHER EXPERIENCE WITH AMINO-ACID THERAPY OF PORTAL CIRRHOSIS IN THE PUNJAB

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In a previous publication (Mallick, Ali and Anand, 1945) the aetiology of Portal Cirrhosis was discussed with special reference to the work of Himsworth and Glynn on rats which suggested the production of cirrhosis due to dietary deficiency of methionine—an amino acid contained in Casein. The results of treatment of 12 cases of Portal Cirrhosis with milk and high protein diet—as judged by the Hippuric Acid liver function test and clinical improvement—were also given which seemed to suggest the important role of Casein in the treatment of this disease. Since then Casein Hydrolysate for intravenous use and Casein Digest capsules for oral use were received through the courtesy of the British Colloids Ltd, Bombay and it was thus possible to give a much more concentrated form of methionine to these patients. The results of the present study are as under.

Method—Ten cases of Portal Cirrhosis were admitted into the medical wards of the V J Hospital, Amritsar, during this period. Their liver function was worked out by the Quick Oral Hippuric Acid test and then all of them were put on Casein. 10 gms of Casein digest powder with 25 per cent added Cysteine was given to them daily by mouth in the form of capsules and this was further supplemented by Casein Hydrolysate given intravenously. At each infusion, approximately 275 cc of the 5 per cent Casein Hydrolysate solution (13 to 14 gms of casein) mixed with the same amount of 10 per cent glucose saline solution was injected slowly by the drip method—the rate being less than 5 cc per minute and a watch being kept for thermal reaction and rigor. In addition they received 2 seers of milk or curd every day. The abdomen was tapped only when absolutely necessary. Rest of the treatment was only symptomatic. In the later stages the supply of Casein capsules being exhausted, the patients were only given injections of Casein Hydrolysate. For the assessment of the results of the treatment, Hippuric Acid liver func-

tion test was employed, in addition to noting the clinical improvement if any

RESULTS

Case I

Bhngat Singh S M 40 years Admitted on 20th August, 1945 Diagnosis —Portal Cirrhosis with Ascites

Condition on admission —Pinched sallow face—extreme anæsthenia—generalised wasting—no jaundice no nnaemin—marked oedema of lower extremities—abdomen very tense with free fluid—dilated veins over abdominal wall—liver and spleen not palpable—dehydration above the region of diaphragm Blood stools urine, normal Urine—Urobilinogen + upto 1 in 60 dilution Van den Bergh—both direct and indirect negative. Icteric index = 4 W R = negative

Treatment and Progress —Symptomatic tapping Casein 2 seers of milk daily

Casein by mouth	Casein Intravenously	Hippuric Acid Test (Normal 2.5 to 8.8 gms.)
22 10-45 to 28 10-45— 70 gms		27 9.45—0 792 gms
29 10-45 to 7 11-45—100 gms	3 11-45— 0 gms	29 10-45—0 843 gms
8 11-45 to 20-11-45—130 gms	16 11-45—13 gms	8 11-45—0 004 gms
21 11-45 to 5-12-45—150 gms	30-11-45—18 gms	21 11-45—1 503 gms
6 2-45 to 9 12-45— 40 gms	7 12-45—12 gms.	6 12-45—1 230 gms
10-12-45 to 16-12-45— 70 gms	22 12-45—18 gms	10-12-45—1 820 gms
17 12-45 to 24-12-45— 80 gms	29 12-45—11 gms	17 12-45—2 084 gms
	6 1-46—18 gms	25 12-45—2 210 gms
12 1-46 to 22 1 -46—110 gms	15 1-46—12 gms	4-1-46—2 004 gms
	22 1-46—18 gms.	11 1-46—2 100 gms.
	5 2-40—13 gms	23 1-46—2 120 gms
		7 2-46—2 278 gms.
		28 8-46—2 041 gms
		17-4-46—2 248 gms
		18-4-46—2 074 gms
		5 6-46—2 281 gms.
Total = 750 gms.	Total = 110 gms	

During the first Casein infusion, when nearly 240 c.c. of the Casein-glucose solution had been infused the patient developed severe rigor and thus further injection had to be abandoned and adrenaline given. In all other infusions on this patient—no ill effects were noted except for the sensation of heat with the temperature never rising above 99°F. Occasionally had rigors which did not come during the infusion but afterwards.

Clinical Progress —General condition gradually improved along with the improvement of liver function. By the beginning of January the oedema from lower extremities disappeared and the fluid in the abdomen accumulated with much less rapidity. On admission he had to be tapped on an average every fifth or sixth day, but now he required tapping only after 8 to 4 weeks. Further improvement in the liver function test as well as the ascites could not be elicited in spite of the casein treatment and thus casein was stopped and the patient kept on milk only. For the next two months his condition neither showed any further improvement nor any deterioration. It was then decided to help him in the establishment of collateral circulation and thus after a blood transfusion of 250 c.c. on the 17th of April "Telma Morrison's Omentopexy" was performed on him by Mr. Hiyaz-i-Qadeer, F.R.C.S. on the 10th of April. Left sided supra umbilical paramedian laparotomy incision was made taking particular care not to damage the collateral circulation round about the umbilicus. The ascitic fluid was mopped out. The antero-superior surface of the liver and the overlying lining of the anterior abdominal wall and diaphragm was roughened by rubbing with gauze and the liver was anchored with anterior abdominal wall by means of through and through stitches. Similarly the diaphragmatic surface of the spleen and the overlying diaphragmatic peritoneum was roughened. At six points the great omentum was displaced into the sheath of the Rectus muscle and anchored there and the great omentum was stitched to anterior abdominal wall for three inches on either side of the incision. A supra pubic drainage tube was put in. The condition of the liver noted at the time of operation was quite interesting. In the words of the surgeon "The liver showed great masses of regenerated tissue over the inferior and posterior aspect and the regeneration was most in evidence over the Caudate and Quadrate lobes. Thus Caudate lobe was seen bulging forward the lesser omentum and the Quadrate lobe was similarly bulging downwards. There was no hob-nailed appearance, but there were white lines coursing over the antero-superior surface of the liver, probably representing the fibrosis. Possibly the process of regeneration over the antero superior surface had masked the fibrotic process."

The post-operative course was uneventful. The suprapubic drainage tube worked well for 3 days but then the drainage stopped. On the 10th day first post-operative tapping was done after which it has to be repeated every second or third week. Following first tapping, he developed oliguria which improved on intravenous glucose saline twice a day. The operation does not seem to have made any difference in the condition of ascites so far—although two months have passed. He still has to be tapped every third week or so. The hippuric acid test also is being maintained at round about 2 gms. i.e. only slightly below the normal figures. He is still in the wards under our care and further progress is being watched.

Case II

Bakhat Shah Singh, S M, 50 years Admitted on 20 10 1945 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission —Pinched face with slight puffiness below eyes—nnaemin present—no cyanosis—no jaundice—slight oedema over feet and lower legs—also slight oedema of abdominal wall—large amount of free fluid in abdomen—abdominal wall greatly stretched—skin over chest and arms dehydrated and wasted—liver and spleen not palpable.

Blood —Hb = 0.6 gms %.—Total R B Cs. = 8920 000/6 m.m. Total W B C. = 8600/6 mm D L C. = Polys = 3% Lymphs = 21% Large monos = 3% Eosinoph = 1% Stools Urine = Normal Urine Urobilinogen + upto 1 in 30 dilution Van-den Bergh = Both direct and indirect negative Icteric index = 3

Treatment and Progress—Symptomatic, tapping, casein, liver extract 2 c c on alternate days, yeast, 2 seers of milk daily

Casein Digest by mouth	Casein Hydrolysate Intravenously	Hippuric Acid Test
28 10-45 to 28 10-45—30 gms	7-11-45—18 gms	21-10-45—1 089 gms
29 10-45 to 6-11-45—80 gms	17 11-45—18 gms.	29 10-45—1 096 gms
8-11-45 to 20 11-45—90 gms	26 11-45—13 gms	8 11-45—1 10 gms
21 11-45 to 27 11-45—40 gms	4-12-45—12 gms	21 11-45—1 635 gms
29 11-45 to 4-12-40—40 gms		28-11-45—1 546 gms
		5-12-45—1 988 gms
Total=280 gms	Total=51 gms.	

After about 5 mts. of the start of the first infusion he felt acute pain in the small of the back and so the infusion was stopped for about 5 mts. The pain subsided and then the rest of the infusion was continued at a slower speed. For the next two days the patient was somewhat off his head and would try to run outside the ward and had to be checked—was alright after two days. In the beginning of the second infusion also there was similar headache but on a lesser duration—the latter two infusions had no ill-effects

Clinical Progress—Apart from the improvement in the liver function test there was not much improvement in his general condition. The oedema from the feet and legs disappeared, but the ascites was there as before and he had to be tapped after every week. He left against advice on 6-12-1945 before further treatment could be given to him.

Case III

Allah Ditta, M M 55 years Admitted on 20 11 1945 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Pinched face—dehydration of chest wall and arm—no jaundice—no cyanosis—anaemia present—very slight oedema over feet—abdomen greatly distended with free fluid—prominent distended veins in the upper region of abdominal wall spleen and liver not palpable—generalised leucoderma present

Blood—Hb=7.2 gms %—Total R.B.C.=3 320 000 a.m.m Total W.B.C.=7 500 c.m.m
D.L.C.=Polys=71%, Lymphos=25%, Large monos=3% Eosinos=1% Stools, Urine—Normal Urine Urobilinogen+upto 1 in 40 dilution. Van-den Bergh=Both direct and indirect negative. Icteric index=4

Treatment and Progress—Symptomatic, tapping, Casein, Liver extract 2 c c on alternate days—milk 2 seers daily

Casein Digest by mouth	Casein Hydrolysate Intravenously	Hippuric Acid Test
29 11-45 to 4-12-45—60 gms	4-12-45—10 gms	28 11-45—1 10 gms
6-12-45 to 18 12-45—80 gms	11 12-45—13 gms	5-12-45—1 231 gms
14-12-45 to 21 12-45—70 gms	20 12-45—12 gms	14-12-45—1 237 gms
		21 12-45—1 455 gms
Total=220 gms	Total=35 gms	

During the first infusion—when about 350 c.c. of the Casein glucose solution had gone in the patient felt a sinking sensation and on examination of his heart, it was found to be having multiple extra-systoles. The infusion was stopped and the extra systoles disappeared within 2 mts. The infusion was again started after about 10 mts. at a slower rate and after about 40 to 50 c.c. were given the extra-systoles and the sinking sensation again appeared. The infusion was again stopped and the extra systoles disappeared. No more was given on that day. In the other two infusions—watch was kept for the extra systoles—but they did not occur. The only ill-effects in the latter infusions were headache and slight nausea with burning sensation in the epigastrium

Clinical Progress—Although the liver function showed only slight improvement the general condition of the patient improved greatly. The oedema over the feet was first to disappear and the ascitic fluid greatly diminished. The patient was tapped only once on admission and when he left hospital there appeared to be only a very slight amount of fluid in his abdomen. Unfortunately he left against advice on 22 12 1945, with a promise to return after a week, but has not turned up since then.

Case IV

Lal Chand H M 40 years Admitted on 11 12 1945 to the Private Wards Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Pinched face—prominent nose marked asthenia—dehydration of arms and chestwall—tongue furred—teeth dirty—no anaemia—no jaundice—no cyanosis—no oedema of feet or ankles—abdomen swollen with free fluid—the abdominal walls not tense—prominent veins in the epigastric region of skin—liver and spleen not palpable

Blood, Urine, Stools=Normal Urine Urobilinogen+upto 1 in 70 dilution Van den Bergh=Direct=Negative Indirect=faintly positive Icteric index=8

Treatment and Progress—Symptomatic tapping once Casein, milk

Casein Digest by mouth	Casein Hydrolysate Intravenously	Hippuric Acid Test
16 12-45 to 24 12-45—80 gms	22 12-45—13 gms	13-12-45—1 205 gms
25 12-45 to 30-12-45—60 gms		25 12-45—1 564 gms
1 1-40 to 6 1-40—60 gms	3 1-40—13 gms	31 12-45—1 75 gms
9 1-40 to 14-1-40—40 gms		7 1-40—2 123 gms.
		15 1-40—2 501 gms.
		20 1-40—2 489 gms.
		16 2-40—2 014 gms
Total = 250 gms	Total = 26 gms	

He had some shivering one hour after the first infusion—controlled by a Irenaline No reaction after the second one

Clinical Progress—The liver function in this case gradually improved to the normal limits. He was tapped only once on the second day of admission when 12 pints of fluid were withdrawn. The fluid reaccumulated after that, but gradually began to be absorbed as the casein treatment was started. He left for his home (local) on 8.1.1946 when there was only very slight amount of fluid in his abdomen and his general condition and wasting had been greatly improved. His re-examination on 15.1.1946 revealed no trace of fluid in the abdomen. His examination at fortnightly intervals since then has not revealed any fluid in the abdomen and he has resumed his normal business. The improved liver function has also been maintained.

Case V

Inayat Ali M.M. 35 years Admitted on 3.1.1946 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Sallow pinched face—no anaemia—no jaundice—no cyanosis—no oedema over feet and ankles—dehydration above the level of diaphragm—abdomen greatly swollen with free fluid—prominent veins over wall—liver not palpable—spleen 2 fingers below costal margin

Blood, Urine, Stools—Normal Urine Urobilinogen + upto 1 in 80 dilution Van-den Bergh—both direct and indirect negative Icteric Index = 3

Treatment and Progress—Symptomatic, tapping, Casein, milk

Casein Digest by mouth	Casein Hydrolysate intravenously	Hippuric Acid Test
8.1.46 to 11.1.46—40 gms	10.1.46—13 gms	5.1.46—0 856 gms
12.1.46 to 18.1.46—70 gms	17.1.46—9 gms	12.1.46—1 840 gms
19.1.46 to 27.1.46—90 gms	24.1.46—12 gms	19.1.46—1 451 gms
		26.1.46—1 819 gms
Total = 200 gms	Total = 34 gms	

Had slight rigor about 2 hours after the first infusion. During the second infusion—first developed backache which disappeared on slowing the flow—later had nausea—finally rigor started and so the infusion had to be abandoned. The third one was uneventful.

Clinical Progress—General condition became better and the fluid in the abdomen became less. It would not fill up so soon as before. Left against advice on 30.1.1946

Case VI

Fauja Singh S.M. 45 years Admitted on 11.3.1946 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Gently emaciated—dehydrated face arms and chestwall—anaemia—no jaundice—no cyanosis—marked oedema over feet and lower legs—abdomen greatly distended with stretched and shining skin—prominent veins seen on abdominal wall—liver not palpable—spleen enlarged upto 4 fingers below costal margin (old history of malaria)

Blood:—Hb = 6.5 gms %—Total R.B.C. = 2,480,000 c.m.m. Total W.B.C. = 8,400 c.m.m. D.L.C. = Polys = 72% Lymphos = 23%—Large monos = 3%—Cosinos = 2% Stools: Urine = Normal Urine urobilinogen + upto 1 in 40 dilution. Van-den Bergh = Both direct and indirect negative Icteric Index = 8

Treatment and Progress—Symptomatic, tapping casein, liver extract 2 c.c. on alternate days milk

Casein Digest by mouth	Casein Hydrolysate intravenously	Hippuric Acid Test
13.3.46 to 22.3.46—60 gms	22.3.46—13 gms	15.3.46—1 591 gms
23.3.46 to 31.3.46—90 gms	29.3.46—6 gms	23.3.46—1 751 gms
		30.3.46—1 040 gms
Total = 150 gms	Total = 19 gms	

During the first infusion he had some palpitation and epigastric discomfort only. During the second one—he started pain in the back which disappeared on slowing the flow. Later on rigor started when only 204 c.c. of casein glucose solution had gone in and so it had to be stopped.

Clinical Progress—There did not appear to be any clinical improvement—inspite of slight improvement in the liver function. The patient left against advice on 2.4.1946

Case VII

Mohammad Khan M.M. 35 years Admitted on 2.3.1946 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Weak—emaciated—swallow pinched face—no anaemia—no jaundice—no cyanosis—dehydration above the region of diaphragm—slight oedema over the feet—abdomen greatly swollen with free fluid—prominent veins over abdominal wall coursing towards chest—liver and spleen not palpable

Blood: Urine and Stools—Normal Urine Urobilinogen + upto 1 in 80 dilution Van-den Bergh—both direct and indirect negative Icteric Index = 4

Treatment and Progress—Symptomatic tapping casein, milk

Casein Digest	Casein Hydrolysate intravenously	Hippuric Acid Test
10.3.46 to 18.3.46—80 gms	10.3.46—9 gms	9.3.46—1 08 gms
20.3.46 to 28.3.46—80 gms	20.3.46—13 gms	20.3.46—1 203 gms
30.3.46 to 5.4.46—70 gms		30.3.46—1 591 gms
6.4.46 to 17.4.46—90 gms	11.4.46—12 gms	6.4.46—1 224 gms
18.4.46 to 27.4.46—40 gms	27.4.46—13 gms	18.4.46—1 040 gms
28.4.46 to 7.5.46—40 gms		28.4.46—1 489 gms
		7.5.46—1 848 gms
Total = 400 gms	Total = 47 gms	

During the first infusion he developed epigastric discomfort which subsided on slowing the rate of flow. Later on when about 300 c.c. had been given—got rigor and so the infusion was stopped. There were no reactions—except for the epigastric discomfort—during the latter infusions—although he had rigor after the stoppage of the infusions.

Clinical Progress—The oedema from the legs disappeared and the general condition improved. The abdomen required tapping weekly before admission to this hospital as well as at the start of the treatment. When he left against advice on 8-5-46 although fluid was present in his abdomen it had not required any tapping for nearly one month. The abdomen was only slightly swollen when he left.

Case VIII

Mohammadi Jauhal M.M. 50 years Admitted on 28-3-1946 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Well built man—no marked emaciation—no anaemia—no jaundice—no cyanosis—no oedema over feet and legs—slight dehydration above the region of the diaphragm—abdomen slightly swollen with free fluid—prominent veins in the skin of epigastric region—liver and spleen not palpable.

Blood Urine Stools=Normal

Urine Urobilinogen + upto 1 in 50 dilution Van den Bergh = Both direct and indirect negative Icteric Index = 5

Treatment and Progress—Symptomatic Casein Milk

Casein Digest by mouth	Casein Hydrolysate Intravenously	Hippuric Acid test
1-4-46 to 5-4-46—50 gms	7-4-46—12 gms	30-3-46—1 530 gms
6-4-46 to 12-4-46—70 gms	11-4-46—13 gms	6-4-46—1 845 gms
13-4-46 to 21-4-46—90 gms	20-4-46—13 gms	13-4-46—1 732 gms
22-4-46 to 2-5-46—40 gms		22-4-46 2 015 gms
		30-4-46—2 415 gms
Total 250 gms	Total 38 gms	

There were no reactions during any of the three infusions except for slight rigor after the first infusion was completed.

Clinical Progress—No tapping was required throughout his stay in the hospital. The swelling of the abdomen gradually became less marked and when he left on 3-5-46—much against persuasions—there was only very slight amount of fluid in his abdomen. Unfortunately it has not been possible to contact him since then.

Case IX

Harbans Singh S.M. 34 years Admitted on 15-5-1946 Diagnosis—Portal Cirrhosis with Ascites.

Condition on Admission—Weak and emaciated—pinched face—anaemic—no jaundice—no cyanosis—slight oedema over feet and lower legs—dehydration above the diaphragm—abdomen greatly distended with free fluid—prominent veins in the wall—liver and spleen not palpable.

Blood = Hb = 3 gms %—Total R.B.C. = 3,520,000 C.M.M. Total W.B.C. = 7,700 c.m.m. D.C.C. = Polys = 72% Lymphos = 25% Large monos = 3% Urine Stools = Normal Urine Urobilinogen + upto 1 in 40 dilution Van den Bergh = Both direct and indirect negative. Icteric Index = 3

Treatment and Progress—Symptomatic, Casein, Liver extract 2 c.c. on alternate days yeast milk Casein Hydrolysate Intravenously

	Hippuric Acid Test
18-5-46—13 gms	10-5-1946—1 264 gms
25-5-46—13 gms	21-5-1946—1 503 gms
5-6-46—13 gms	29-5-1946—1 414 gms
	9-6-1946—1 935 gms
Total 39 gms	

Note—Casein Digest capsules were not given as the stocks had finished.

During all the infusions he had headache and slight palpitation—rigors two to three hours after infusion. On the second day after the third infusion he developed rise of temperature and great discomfort and distension of abdomen due to flatulence. This lasted for two days and then subsided.

Clinical Progress—There was only slight improvement in his general condition. Oedema disappeared from the feet. Abdomen was tapped only once on admission and although large amount of free fluid was still there in abdomen it did not require any further tapping. Left against advice on 12-6-1946.

Case X

Rahim Bux, M.M. 35 years Admitted on 15-6-1946 Diagnosis—Portal Cirrhosis with Ascites

Condition on Admission—Not much emaciated—pale pinched face—anaemic—no jaundice—no cyanosis—dehydration above the level of diaphragm—slight oedema over feet—abdomen distended with free fluid—prominent veins in the epigastric region—liver not palpable—spleen enlarged upto 6 fingers below costal margin (old history of malarial fever).

Blood = Hb = 10 gms %—Total R.B.C. = 4,120,000 c.m.m. Total W.B.C. = 6,800 c.m.m. D.L.C. = Polys = 71% Lymphos = 21% Large monos = 1% Eosinoph = 1% Urine stools = normal Urine Urobilinogen + upto 1 in 70 dilution Van den Bergh = Direct—negative Indirect—slightly positive Icteric Index = 0

Treatment and Progress—Symptomatic tapping Casein Liver Extract 2 c.c. on alternate days milk

Casein Hydrolysate intravenously	Hippuric Acid Test
18-5-1946—13 gms	16-5-1946—0 701 gms
25-5-1946—13 gms	21-5-1946—1 215 gms
5-6-1946—9 gms	29-5-1946—1 440 gms
	9-6-1946—1 795 gms
Total 35 gms	

At the start of the second infusion he had great nausea and vomited—the injection was stopped for 5 mts and restarted at a slower speed. During the third infusion after about 800 c.c. had gone in—developed rigor and so the infusion had to be stopped.

Clinical Progress—The general condition of the patient showed improvement. Oedema from feet disappeared but there was no diminution in the ascites—tapping required at weekly intervals. Left against advice on 13.6.1946.

TABLE
10 Cases of Portal Cirrhosis with Ascites

Case No	Van-den Bergh Reaction	Icteric Index	Urine Urobilinogen (dilution upto which—)	Cesoin Digest by mouth	Cesoin Hydrolytic intra venously	Hippuric Acid Test on admix sion (Normal = 2.5 to 3.3 gms)	Hippuric Acid Test after treatment	Clinical improvement after treatment
1	Negative	4	1 in 60	gms 750	gms 110	gms 0.843	gms 2.281	General condition much better. Ascites diminished (Remarks: Telma Morrison operation done.)
2	Negative	3	1 in 30	280	51	1.080	1.089	Not much improvement in general condition or ascites.
3	Negative	4	1 in 40	220	35	1.10	1.455	Great diminution in ascitic fluid.
4	Indirect†	8	1 in 70	250	20	1.203	2.014	Marked improvement in general condition. Ascites disappeared.
5	Negative	3	1 in 70	200	74	0.850	1.819	Ascites less than before.
6	Negative	7	1 in 40	150	10	1.501	1.910	No clinical improvement.
7	Negative	4	1 in 30	100	47	1.08	1.848	Ascites less than before.
8	Negative	5	1 in 30	250	38	1.570	2.411	Ascites greatly diminished.
9	Negative	3	1 in 40	Stock finished	70	1.264	1.915	Slight improvement in general condition and ascites.
10	Indirect +	9	1 in 70	do	15	0.761	1.993	Not much clinical improvement.

DISCUSSION

Experimentally, two distinct lesions in the rat's livers have been produced by dietary irregularities (Himsworth and Glynn, 1944), (Witts, 1945).

(a) Diets containing excess of fat or deficient in lipotropic factor produce fatty infiltration of the liver. Long continued fatty infiltration eventually leads to diffuse hepatic fibrosis and cirrhosis of the Laennec type, presumably by interfering with the nutrition of the cells. This can be prevented by giving lecithin or choline (which is a constituent of lecithin). The inference is that the body needs lecithin to transport the fat away from the liver, and it cannot manufacture lecithin unless it is supplied with choline. Fatty infiltration can also be prevented by giving methionine (or casein which contains methionine). It is claimed that the methionine prevents fatty infiltration because it provides the methyl group for the manufacture of choline.

(b) On the other hand low protein diets have quite a different effect on the liver. These produce massive hepatic necrosis (Trophopathic Hepatitis) with its sequelae of fibrosis and nodular hyperplasia, thus producing a picture indistinguishable from that of portal cirrhosis. This necrosis cannot be prevented by choline, but can be prevented by methionine and to a less extent by cystine, and cysteine, the three amino-acids having the common property of containing sulphur. It is claimed that the sulphydryl (SH) radicle prevents necrosis. These three thio-amino-acids also claimed to exert considerable protection against liver poisons, such as chloroform, carbon tetrachloride and organic arsenicals.

Thus it appears that methionine is a key substance in the life of the liver, as it contains the labile methyl group which protects against fatty infiltration and cirrhosis, and the sulphydryl group which protects against massive necrosis and nodular hyperplasia. Choline only protects the liver against fatty infiltration, while it has no effect against necrosis. It is even claimed that choline facilitates the production of massive necrosis (Himsworth and Glynn 1944). Cystine though it can slightly protect the liver against necrosis, on the other hand seems to encourage fatty infiltration.

These observations find support in the experimental works of Rich and Hamilton (1940) who claim to have produced hepatic cirrhosis in rabbits fed on a diet deficient in some unknown factor present in yeast—the diets however containing a fairly large amount of fat which is not the natural diet of the rabbits. Machella and Maguire (1940) repeated this experiment on albino rats with negative results. Blumberg and McCallum (1941) produced cirrhosis of liver in rats fed on a high fat diet which was prevented by giving choline along with fatty diet. Lillie et al (1941) on the other hand have observed cirrhosis of liver in some of the rats placed on a diet low in proteins and sulphur containing amino-acids. Rao (1942) has noted cirrhosis of the liver in some of the monkeys placed on a "Poor South Indian diet" consisting mainly of rice. Gillman (1944) produced cirrhosis by giving rats a diet similar to the one consumed by natives of Rand (South Africa), consisting mainly of maize.

The controlled clinical trials with these dietary factors in the treatment of infective hepatitis, post-arsenical jaundice and homologous serum jaundice have proved a failure—Darmady (1945), Higgins et al. (1945), Wilson et al (1945), Peters et al (1945), Richardson (1945), Turner et al, (1945). This was but to be expected as here one is dealing not with a disease of dietary deficiency but with infection of the liver. On the other hand the dietary treatment of the cirrhosis of the liver is highly promising. Patek (1937, 1943) put his cirrhosis cases on a diet rich in protein and ample in carbohydrate and fat which consisted largely of meat, milk and eggs. Twenty of his 54 patients, treated in this way, showed signs of "clinical recovery". Snell (1940) modified the Patek regime and gave a diet containing 500 gms Carbohydrate, about 60 gms fat and 100 gms protein, derived from sources other than meat like milk, egg white vegetables and wheat, supplemented by crude liver extract and yeast.

His results seem to be equally as promising as those achieved by Patek Rao (1946) has reported "clinical recovery" of two patients out of a series of 108 treated with rich diet only—although both these returned later on with their abdomens again full of fluid. Ten out of the 12 cases of portal cirrhosis treated by us last year on high protein diet—chiefly in the form of milk—showed definite improvement in their liver function. Three of these had "clinical recovery" as judged by the disappearance of ascites while the rest seven had slight "clinical improvement" only. Beams (1946) treated 20 cases of cirrhosis of the liver with a high protein (110 gms from meat, vegetables and dairy products), low fat (50 to 70 gms) and carbohydrate (250 gms), supplemented with 30 to 45 gms of brewers' yeast and a combination of choline and cystine, (2 gms each daily). 12 of the 20 patients with livers which were not enlarged showed no response to therapy, whereas 7 of the 8 patients with large livers made a good recovery from liver decompensation with disappearance of ascites and increase in serum albumin. 15 other patients of cirrhosis of the liver with enlarged livers were treated only with high protein, low fat diet supplemented with yeast only but no choline or cystine and these did not show recovery. Thus he concluded that the combination of choline and cystine has a favourable influence in the treatment of cirrhosis. The striking difference in the response of patients with large livers compared to patients with livers not enlarged suggests that the combination of choline and cystine is effective where fatty changes in the livers are suspected. Russakoff and Blumberg (1944) have reported a personal communication from Gordon—who observed striking improvement in 5 cases of alcoholic cirrhosis treated with a combination of choline and cystine.

In the present study the high protein diet (chiefly in the form of milk) was continued and was further supplemented by digested and hydrolysed casein in order to provide methionine in a more concentrated form. As discussed above methionine is the amino-acid of choice in the treatment of portal cirrhosis, as it protects the liver against both necrosis and fatty infiltration—while on the other hand choline can prevent only the fatty infiltration and cystine can slightly protect against necrosis and thus both have to be given together. The liver function (assessed by the Hippuric Acid Test) showed gradual and steady improvement in all the cases treated though it reached the normal limits only in case No 4. Although there does not seem to be any definite relationship between the improvement in the liver function and the amount of casein given (see tables) the improvement in each individual case became more marked as more casein was given. There was also a corresponding "clinical improvement" as judged by the general condition of the patient and the diminution in the amount of the ascitic fluid or its reaccumulation after a longer interval after tapping. Case No 4 only showed complete "clinical recovery". He has been under observation for nearly six months now and has not got any recurrence. Cases No 3 and 8 had a very slight amount of fluid in their abdomen when they left against advice and it is to be inferred that this too would have

disappeared had they carried on the treatment a little longer. Other cases—except No 1—also left against advice with variable amounts of improvement. The treatment being a long drawn out one and the majority of the patients being illiterate, it has not been possible to keep them in the hospital for more than a month or two in spite of persuasions and this also explains the impossibility of following them up when they left. Case No 1 has shown marked improvement of his liver function which increased from very low figures to a little below the normal level. It has not been possible to cause further improvement. His general condition improved greatly but the ascites though much less in quality is still persisting, in spite of the attempt to establish collateral circulation by the "Telma Morrison's omentopexy". He is the only patient in whom liver was examined after the casein treatment had been given and it is interesting to note the great regeneration of the liver especially marked over the Caudate and the Quadrate lobes.

The stage of the disease in which any patient comes must also be borne in mind when judging the results of the treatment. At any stage of the disease, we are dealing with normally functioning liver cells, diseased liver cells and fibrous tissue. Methionine exhibited in adequate amounts could only preserve the residual normal liver tissue and prevent further damage of the affected cells but could have no action on the fibrous tissue. One can reasonably expect complete "clinical recovery" only in those cases which come in the early stage of the disease. Thus the results of the present investigation judged from this angle are in conformity with what was expected.

Lastly a few lines regarding the intravenous infusions of casein hydrolysate. Before sending us this stock, it had been tried by Professor J Beattie of the Bernhard Baron Research Laboratories, London and the Medical Research Council, England. Although Professor Beattie found very few reactions, the M R C people found a high incidence of feverish reactions (Mr Proe of the British Colloids Ltd --personal communication). We have been following the technique employed by Professor Beattie and in all our trials there have been no feverish reactions, except case No 9, who developed fever and abdominal distension one day after the last infusion, lasting for two days. Rigors have been quite common and sometimes backache which would disappear on slowing the rate of administration. Occasionally there was nausea with abdominal discomfort and once vomiting and sometimes feeling of palpitation. In one case during the first infusion only, there was sinking sensation and multiple extra-systoles (cause?) while in the latter infusions these did not appear. Thus the stuff is quite safe to be administered provided due aseptic precautions are taken and the rate of administration is quite slow.

Though with study of a limited number of cases, it is not possible to draw any definite conclusions, yet in the case of a prolonged malady with a variable course and a hopeless outlook, the clinical recovery and improvement of even a few cases is worth consideration and serious thought as it may open a new era in the prophylaxis and treatment of portal cirrhosis. Provided the disease is detected

in the early stage by the various delicate hepatic function tests and attacked by all the measures at our command (high protein diet with preponderance of milk, administration of casein hydrolysate or choline and cystine combination and blood transfusions if possible), we may legitimately cherish that it will present a much more hopeful outlook than has been possible hitherto

We are grateful to the British Colloids Ltd Bombay (Mr Ernest Proe Manager) for the supply of casein digest and casein hydrolysate free of cost. Our thanks are also due to Colonel D Clyde C.I.E. I.M.S., Inspector General of Civil Hospitals Punjab for the funds placed at our disposal and the Medical Superintendent and the Staff of the V J Hospital Amritsar, and the Physiology Department of the Glancy Medical College, especially Mr G M K Baloch M.D. and Mr Rafique Ahmad M.B.B.S., for their help and co-operation and Mr Riaz I Qadeer, F.R.C.S. for kindly performing Talmor Morrison's Omentectomy on one of our cases.

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OXYGEN ADMINISTRATION

THE ORO-PHARYNGEAL CATHETER METHOD

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Before I actually describe the oro-pharyngeal method of oxygen therapy I would like to say a few words about the principles and purposes of oxygen therapy

Oxygen is necessary for all higher forms of life and while the lungs and the circulation provide a transport system for oxygen from the external air to the tissues, the most important factor is the oxygen pressure in the immediate neighbourhood of the cell. Any disturbance in the oxygen pressure in the tissues will therefore naturally interfere with the proper oxygenation of the cells. Experiments have been conducted to determine directly how the gas pressures in the tissues will be affected by various abnormal conditions of clinical interest, for example, haemorrhage, hoemolysis, exposure to carbon monoxide gas, exposure to low oxygen pressures in the inspired air and exposure to high oxygen pressure as in oxygen therapy. The relative changes in oxygen pressures in the tissues under various conditions are shown in Fig 1. From this it can be seen that bleeding hoemolysis, breathing oxygen at low

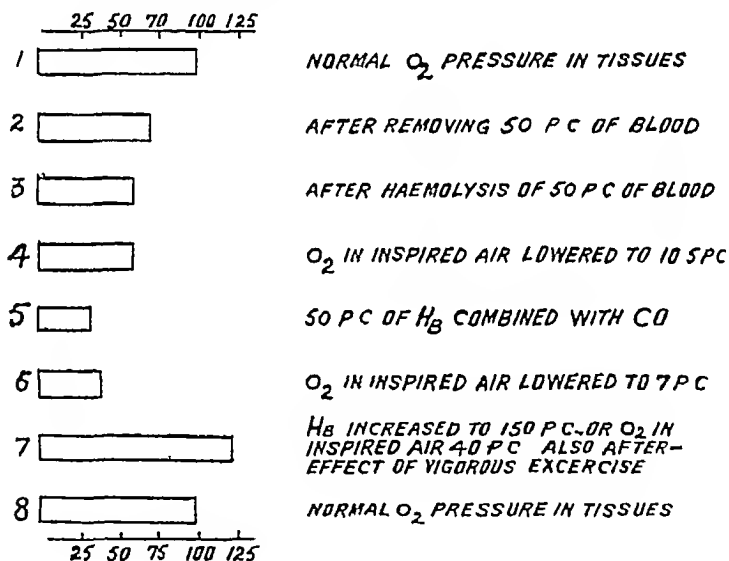


Fig 1

pressure and carbon monoxide poisoning decrease the oxygen pressure in the tissues whilst breathing oxygen as in oxygen therapy at increased pressure upto 60 per cent of an atmosphere, increases the oxygen pressure in the tissues. This increase in oxygen pressure in the tissues establishes the scientific basis for oxygen therapy.

A paper read at the 59th Meeting of the Seth G S Medical College and K E M Hospital Staff Society Bombay on May 11 1940 with Dr R G Dhayagude in the chair

The purpose of oxygen therapy is to overcome oxygen want due to some interference with proper oxygenation of blood, as in pneumonia, coronary thrombosis, congestive heart failure, emphysema or atelectasis. In the presence of fever the metabolism is increased and the oxygen want is thereby increased. Therefore if the patient is to be benefited, the amount and concentration of the oxygen employed must be sufficient to increase the oxygen pressure in the tissues. It is important that the physician prescribe definitely the concentration of oxygen to be breathed by the patient, just as he prescribes the dose of drugs. The optimum range of oxygen concentration will vary in different patients. In some cases 30 per cent will be adequate to correct the deficiency, in other instances as high as 70 per cent may be required.

TABLE 1
Comparison of some of the Methods for Oxygen Therapy

	CHAMBER	TENT	ORO-PHARYNGEAL CATHETER
Initial cost	Very high machinery for cooling and circulation necessary	Moderate a tent costs nearly one thousand rupees	Low, Rs. 250 will buy a reducing valve, humidifier, tubing, etc.
Cost to maintain	High service and repair cost considerably	Moderate Rs. 50 per day as worked out at Tata Hospital	Low, Rs. 15 per day and there is little to replace except catheter
Nursing care	Usually a nurse or attendant must be present at all times	A patient requires more attention in a tent. Nursing care is impeded	Patient requires very little attention after a catheter has been inserted
Oxygen concentration	A concentration of 100% is possible though not usually reached	60% can be supplied with a heavy flow of oxygen	60% can be supplied with a flow of 6 liters per minute
Possible ill effects	Fire is a hazard. Frequent analysis should be made to avoid low oxygen and high carbon dioxide atmospheres	Asphyxia is possible if oxygen flow is cut off accidentally. The soda lime may become exhausted accumulating a high CO ₂ content	Carelessness may permit insufflation of water

Practically all hospitals have at present some sort of equipment whereby oxygen may be administered to a patient. The economic factor has hindered the more generalised acceptance and the use of this form of therapy. According to Waters and his associates an oxygen therapy service in a modern hospital should fulfil at least four requirements, namely

- (1) It should be clinically and scientifically efficacious,
- (2) It should be readily available for a number of patients at any time,
- (3) It should be simple in technic,
- (4) It should be economical

Though there are various technics for the administration of oxygen therapeutically, namely, the chamber, the tent and the various types of face masks, the oro-pharyngeal catheter method is rapidly becoming more commonly employed. A comparison of the common methods for oxygen therapy is shown in Table 1. From

this it can be seen that the oro-pharyngeal method is the simplest, economical and most easily available of all appliances

The purpose of this paper is to describe in detail the oro-pharyngeal catheter method of oxygen therapy with a view if this method of oxygen therapy could be used as a standard technic at the K.E.M. Hospital

The description of the technic as used may be divided into two sections, namely, (1) Apparatus, (2) Technic of placing the catheter

Apparatus—Large supply cylinders should be used as they obviate the necessity for frequent changes They are easily transported on small trucks (Fig 2), which even a nurse can handle without undue effort It is not necessary to use medical oxygen, com-

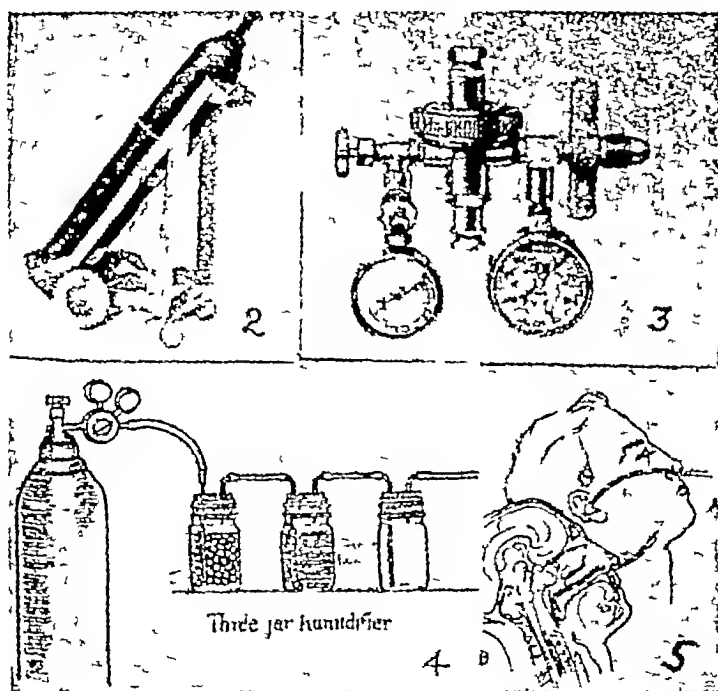


Fig 2 3 4, and 5

mercial oxygen has been found satisfactory also A 165 Cu ft oxygen cylinder lasts about 18 to 20 hours and the price of oxygen is somewhere about Rs 10 These cylinders should be equipped with reduction gauges which not only register the amount and pressure of oxygen in the cylinder, but also estimate the flow of oxygen in litres per minute (Fig 3) By regulation of these gauges the desired flow from one to fifteen liters per minute of oxygen may be obtained

Since dry oxygen is somewhat irritating to mucous membrane, a humidifier should be used Where there is excessive pulmonary secretion, it is better to omit the humidifier to aid in drying up the secretion In order to humidify the oxygen adequately it should

be broken up into fine bubbles, thus presenting more absorptive surface to the water. A simple apparatus is one in which the oxygen is discharged into a small container full of beads or into a small carbon dome. A water flow meter may be incorporated into the humidifier by allowing the oxygen to bubble through a small tube with graduated holes down the side which is immersed in a similar jar filled with water. In this manner the oxygen flow may be more accurately measured in that it estimates the actual delivery flow. It is safer to install an empty bottle between the humidifier and the patient to function as a trap (Fig 4). This third jar or trap may be avoided if a guard in the form of a small sheet of metal is placed at the top of the tube for the bubbles to strike against. These two jars can be yoked firmly together and small arms attached so that the humidifier may be hung on a bed as well as set up right on a side table.

For insufflation a soft and pliable urethral catheter size F 10 to F 12 should be used. Since a single stream of oxygen will irritate the throat by striking one small area of mucous membrane, extra holes should be punched in the half-inch nearest the tip by means of a red-hot safety pin. There is now available a catheter prepared especially for oxygen therapy in the wanted sizes and with the desired perforations. Temperature regulating devices are unnecessary for this technic of oxygen administration. The oxygen enters the patient's oro-pharynx at approximately room temperature.

Technic of placing the catheter —The efficiency of this technic is entirely dependent upon the proper placement of the catheter in the oro-pharynx. Oxygen is blown out through the other nostril when it is insufflated into naso-pharynx. With the entire equipment assembled and tested, the depth the catheter is to be inserted is measured approximately. The distance ($4\frac{1}{2}$ to $5\frac{1}{2}$ inches) between the external nares and the tragus of the ear has been determined to represent the average depth the catheter is to be inserted. It is best to mark the catheter with a bit of adhesive tape before it is inserted. Every catheter has its natural curve and it is inserted with this natural bend down so that it may fall along the floor of the nose and not be in contact with the more sensitive upper portion. Before insertion the catheter should be lubricated with a thin film of vaseline. The stream of oxygen should be started before the catheter is inserted to discover possible incorrect connections.

If the patient is conscious then he lies flat, with the head resting on a comfortable pillow, and held so that the mandible makes approximately a right angle with the body. The patient is then instructed to breathe through the mouth at a normal rate. The catheter is gently and slowly passed through the nares to the depth previously determined by measuring from the nares to the tragus. The catheter is held in this position for a few seconds, and then introduced beyond the measured depth to a point where the patient is seen to make swallowing movements. Swallowing indicates the catheter is placed with its tip too close to the oesophagus. The catheter is then withdrawn slightly to a point where deglutation is

TOXICITY OF OXYGEN

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Shortly after having isolated oxygen, Priestley (1775) wrote "from the greater strength and vitality of the flame of a candle in this pure air, it may be conjectured that it might be peculiarly salutary to the lungs in certain morbid cases. But perhaps we may also infer from these experiments that though pure dephlogisticated air might be very useful as a medicine, it might not be so proper for us in the usual healthy state of the body, for as a candle burns out much faster in dephlogisticated than in common air, so we might, as may be said, live out too fast and animal powers be too soon exhausted in this pure kind of air. A moralist at least may say that the air which nature has provided for us is as good as we deserve." So even Priestley felt that oxygen administration might be attended with some danger. Subsequently, Lavoisier (1783) observed the toxic effects on guinea-pigs when kept in "vital air". Some years later Beddoes (1796), one of the earliest advocates of the therapeutic use of oxygen (O_2) deprecated its injudicious use as likely to cause pulmonary damage. He was inclined to believe that it was not deficiency but excess of oxygen which was pernicious. Since then a number of observers in various countries have carried out experiments on different animals (dogs, turtles, pigeons, rats, guinea-pigs, cats and monkeys) in varying numbers and all of them are agreed that excess of oxygen has a poisonous effect on animals. They, however, disagree as to the concentration of oxygen at atmospheric pressure needed to produce toxic effects and the length of time of administration, but are all impressed by the variation in susceptibility of individual animals. Clamann and Becker-Freysing (1939) maintain that there is an inverse relationship between the size of an animal and its susceptibility to the deleterious action of oxygen and this is claimed as being related to the lower metabolism of large animals in terms of their body surface.

When concentration of oxygen at atmospheric pressure is greater than 60 per cent, toxic effects are produced, and when over 70 per cent, it proves actually poisonous in the case of dogs, rabbits, guinea-pigs and mice but in a varying form from 2 to 10 days if by then death does not supervene. The manifestations are drowsiness, anorexia, loss of weight, dyspnoea, cyanosis, restlessness, spasms of the muscles and limbs, convulsions, unconsciousness and death from lack of oxygen because of destructive lesions produced in the lungs. These changes in the lungs are not characteristic of an infectious process and are interpreted as possible protective reactions, which, progressing too far, cause death. On post-mortem examination the following changes are found: inflammation, congestion, oedema, atelectasis, fibrin formation and consolidation in the lungs, pneumonia of various types, bronchitis with bronchiectasis, hypertrophy and hyperplasia, desquamation and degenerative changes in the alveolar cells.

Long accumulation of experimental data hardly leaves any doubt that continuous exposure over 12 to 14 hours or even less to

oxygen in concentration above 60 to 70 per cent atmospheric pressure results in pathological changes particularly in the lungs and, if the exposure is further prolonged, the changes frequently prove fatal. The onset of the noxious effect on man may be delayed more than in other animals but there is good reason to believe that the human animal is similarly affected.

How toxic effects are produced—Bert (1878) who was one of the first to recognise the toxic effects, attributed them to oxygen alone, but later workers discovered factors other than high oxygen pressure. Oxygen administered at a high pressure has a predilection for producing changes in the lungs. As already mentioned this has been noticed in animals by a number of observers. The changes vary from a mild congestion to oedema, epithelial degeneration and desquamation, fibrin formation and finally pneumonia disturbing the normal removal of the carbon dioxide from the blood. The vital capacity is diminished in human beings. Oxygen therapy may also have toxic effects directly on the brain, through a disturbed metabolism or failure of removal of metabolites. Recent work has revealed degenerative changes in the brain of an animal dying of oxygen poisoning. Another causative factor may be increase in carbon dioxide tension in the tissues. This is brought about by non-reduction of oxyhaemoglobin when it comes in contact with the tissues as there is a large quantity of oxygen dissolved in plasma which becomes available to the tissues, leaving oxyhaemoglobin intact. Hence there is no reduced haemoglobin for carbon dioxide to combine with and carry to the lungs for removal. In the lungs there is probably interference due to changes which occur as a result of high oxygen therapy. This further contributes to increased carbon dioxide tension. But the carbon dioxide and its disturbed transport by the blood cannot be considered as the major cause. Because of increased carbon dioxide tension in the tissues the reaction in them might be more on the acid side adding another factor in toxic effects. Tissue acidity might decrease metabolism but high oxygen therapy has a depressing action on the enzymic systems, cellular reactions and respiration, and involves the risk of poisoning. This combined with what has been described above may prove an aetiological factor in the production of toxic effects, if not actually the ultimate cause of the toxic action of high oxygen therapy. An animal poisoned by high oxygen therapy may be said to be drowned in oxygen.

Toxic effects in Human Beings—Because of the recent introduction and widespread use of apparatus designed to deliver 100 per cent oxygen, it is highly important that results of well-controlled experiments on man be reported in order to determine the limits of safe oxygen usage in therapy. Behnke (1940) found that in healthy men, 99 per cent of oxygen administered for 7 hours produced symptoms of distress. Some, however, tolerated it for as long as 17 hours. Becker-Freysing and Chamann (1939) carried out more complete investigations on 2 men breathing 90 per cent oxygen for sixty-five hours. They found the vital capacity reduced in both cases and that one had developed nausea, repeated vomit-

ing, tachycardia, afebrile tracheobronchitis, dyspnoea and pain in the elbows or knees Boothby et al (1939) employed 100 per cent oxygen continuously for 48 hours on more than 800 patients without toxic effects Evans (1944) too, never observed any untoward effects in more than 800 patients receiving 100 per cent oxygen therapy Recently Comroe et al (1945) observed the effects of 98 to 99.5 per cent oxygen in a large number of young men over a period of 24 hours using controls and frequently analysing mask air to ascertain the percentage of oxygen The toxic effects observed by them were as follows —

(1) Substernal distress—28 out of 54 men complained of this symptom which they described as aches, choke, or "felt like bronchitis," which appeared on an average about 14 hours after the commencement of the oxygen administration, the range being from four hours to twenty-two In the majority of the cases the distress was felt in the mid-sternal region, but in some it radiated to the arm From the experiments by various workers it was found that the concentration of oxygen required to produce symptoms in normal men was between 50 and 75 per cent A 60 per cent level is estimated as probably safe by Bean (1945) and by Stadie et al (1944), who also found that as regards the total incidence of symptoms (mild, moderate or severe) there was seemingly no significant difference between those given 100 per cent oxygen continuously or with intermissions

(2) Forty-three per cent of those breathing 100 per cent oxygen continuously developed nasal congestion or coryza during the first 24 hours

(3) Conjunctival irritation occurred in about a quarter of the cases due to irritation caused by oxygen

(4) There was a significant decrease in their vital capacity in men breathing a higher concentration of oxygen This fact evidenced alveolar damage In view of such damage that occurs in animals with longer exposure to 100 per cent oxygen it is believed that the cases in question had signs of early pulmonary irritation

(5) Some of the subjects developed discomfort in the ears and others felt an unusual degree of fatigue

There was hardly any change in formed elements of blood

As will be seen there is unanimity amongst workers about toxicity of oxygen when given to animals in high concentration for a length of time, but there is no agreement whatsoever among clinical investigators concerning the harmful effects of oxygen on man Booth and Evans consider it harmless even when breathed in concentration of 100 per cent for 48 hours or longer while Behnke, Comroe and others have definitely showed that it produced toxic effects These varying results are explained by the presumption that oxygen administered by masks and other methods has a concentration of 100 per cent This level may in reality not be attained for the following reasons

(1) The person's intake of oxygen through a mask may be from 40 to 95 per cent depending on whether the mouth is open or closed In some cases such delivery involves partial re-breathing through a

reservoir bag The mask has to be removed for feeding, drug administration, or nursing care, it may not fit the face properly or may easily be displaced in sleep or removed either deliberately or unconsciously by anoxic patients

(2) As in the case of animals there appears to be a factor of individual variation, some subjects having severe symptoms while a few have none at all The susceptibility of individuals varies, the lower the metabolism the more susceptible the animal

(3) Another explanation of the failure of clinicians to observe the toxic effects of high oxygen concentration is that patients with pneumonia or coronary occlusion being uncomfortable as a result of the pain of pleurisy or of cardiac ischemia, the substernal discomfort produced by oxygen is overlooked

In spite of some reports that continuous breathing of pure oxygen is innocuous, the accumulated evidence from animal experiments (including those on man) indicates that continuous administration of pure oxygen at atmospheric pressure, even for periods of a few hours, is attended with danger of pulmonary damage, particularly in individuals with diseases of the lungs and, therefore, demands the exercise of caution Clinicians must accordingly bear in mind that oxygen is a drug to be used in accordance with well-recognised pharmacological principles, i.e., having certain toxic effects and not being completely harmless (as is widely believed in clinical circles), it should be given in the lowest dosage or concentration required by a particular patient

There are three main groups of indications for oxygen therapy

(1) to combat arterial anoxaemia, (2) to hyperoxygenate the blood in conditions not associated with anoxaemia (coronary occlusion, fever, migraine, polycythaemia and so on), and (3) to eliminate nitrogen from the body (in diving)

The rational use of oxygen in anoxaemic states should be governed by measurements of arterial blood oxygen saturation The technique of arterial puncture is easy and the determination of arterial blood-oxygen saturation by the Van Slyke method is simple and should be used much more widely than it is done When administration of sulphonamides, penicillin or atabrine is controlled, these days, by estimation of their concentration in blood, that of oxygen concentration in blood is never done

In the first group above it can easily be administered by a periodical check of oxygen saturation in arterial blood, 100 per cent oxygen being given for the first few hours and later decreased to 50 to 60 per cent, unless found insufficient to oxygenate the blood

In the second group, hyper-oxygenation is required and therefore 100 per cent oxygen should be administered, but the patient should be asked periodically about the symptoms by way of indications-guide

In the third group, oxygen administration is hardly required for more than a few hours and the question of toxic symptoms rarely arises

This must not deter any one from using oxygen when indicated It, must, however, be borne in mind the toxic effects mentioned

above which may occasionally arise from its administration, particularly in susceptible persons and more so with lung diseases. The writer feels that the only way of avoiding these toxic effects of oxygen therapy is by repeated controls. The control is frequent estimations of oxygen saturation in arterial blood.

Here is the report of a case in which symptoms of oxygen toxicity seem to have occurred.

A boy aged 20 who for ten days had profuse and repeated haemoptysis was admitted in the K E M Hospital for treatment, as he had developed consolidation of the upper half of the right lung. He was given continuous oxygen through a nasal catheter at a rate of about 2 litres per minute. Three days later he became drowsy and developed peculiar movements. He began lifting up his head and trying to sit up. Later he became unconscious and contractions spread to all the muscles of the body, the spasms being more marked in the flexor group of the muscles. These movements were controlled by sedatives in progressively increasing quantities. The patient remained in this state (unconscious with spasms) for 10 days. It was felt from absence of cyanosis at this stage that further administration of oxygen was not necessary and it was discontinued. Shortly afterwards the patient regained consciousness and the spasms subsided. A subsequent X ray of the chest disclosed that the consolidation had extended to the whole of the lung on the right side and to a small patch on the left side. Cyanosis was present. Oxygen was given again continuously. During this treatment he became drowsy once again and 24 hours later he complained of substernal pain. Spasms recurred. Oxygen was discontinued and symptoms subsided. The patient complained of nasal catarrh and laryngeal irritation. He died a few days later of general exhaustion. A post mortem examination was not available.

In this case the appearance of the above-mentioned symptoms on administration of oxygen, and their disappearance on withdrawal might necessarily lead one to assume that the symptoms in question were due to the toxic effects of oxygen. There is, however, no direct proof, as the arterial blood oxygen saturation was not estimated. It is quite possible that the patient was susceptible to the effects of oxygen.

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Dr V P Mehta enquired whether oxygen administered intravenously and by the B L B mask had any advantage over the oropharyngeal method. He also added that obtaining a sample of blood from any artery for estimation of oxygen saturation, was not a difficult procedure.

Dr B N Sircar disagreed with Dr J C Patel that oxygen administered by the oro pharyngeal method produced toxic effects. He was of the opinion that in the case cited by Dr Patel the toxic symptoms were due to some other cause.

Dr J C. Patel replying to Dr Dhurandhar said that the irritation of the eye was produced by oxygen coming into contact with the conjunctiva when it was administered by the B L B mask. He added that the criteria for oxygen requirements should not depend on the presence of cyanosis and increased pulse and respiration rate but on the estimation of the oxygen saturation of the arterial blood. This procedure was not difficult and could be carried without incurring additional expenditure by the Physiology Department of any well organized institution.

CIRCULATORY FAILURE AND ITS TREATMENT

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(Continued from page 223)

Treatment of left ventricular failure

Rest—Rest in bed for a few days, preferably for several weeks, is imperative in these cases and affords great relief. If the patient is orthopnoeic, it is no good trying to make him lie down as it only serves to increase his distress, he should be supported or propped up with pillows in the most comfortable position possible. In some cases the patient is best off with a cardiac-table in front of him, where he can rest his arms. It is a common sight to see these cases of left-sided failure tossing about in bed trying to find some position that may afford relief to their dyspnoea. Rest in bed, though essential in these cases, does not afford relief to the same extent as in cases of right-sided failure of the heart. In the latter type of case, response to rest is often dramatic, the oedema tends to disappear, the urinary output shows an increase and the symptoms lessen in severity. In left-sided failure, rest in bed is not so successful, probably for the following reasons.

The rate of the heart is frequently normal or only moderately raised in cases of left ventricular failure, with the result that rest in bed can cause but a small change in heart rate. The reduction in the work of the heart (as the result of the rest) is therefore correspondingly negligible.

When put to bed, the subject of left-sided failure is seldom able to lie quietly or maintain the recumbent position, instead, he is usually restless and sits up in bed (as a result of the dyspnoea) thus neutralizing the beneficial effects of confinement to bed.

A low caloric diet is beneficial in these cases, but should not be kept up for too long. Some physicians put the patient on a Karell diet for two or four days to begin with, this consists of 200 c.c.s of skimmed milk given four times a day. This is followed up by a diet supplying about 1000 or 1500 calories a day. Cardiac patients in India are seldom tolerant of the exclusively milk diet advocated by Karell. Besides finding it distasteful, they complain of abdominal discomfort and excessive flatulence. If milk is strongly indicated in an individual who is more or less intolerant of it, then boiling, peptonisation or citrate treatment of milk may be tried in order to facilitate digestion.

The dietary of cardiac cases is an individual problem depending on the type of individual, the state of nutrition of the individual, the nature of the disease, the tolerance of the individual to various articles of diet etc. The following generalizations may facilitate the construction of dietaries for the use of cardiac cases.

Since gastric distension, owing to the nearness of the heart to the stomach, is capable of exerting a deleterious effect on the normal functioning of the heart, all efforts should be made to prevent such distension. Meals of relatively small bulk are indicated. There is a tendency on the part of people, on reducing or low-caloric diets to

take only one (large) meal a day, such a habit should be discouraged in cardiac cases, since the large bulk of the meal will doubtless distend the stomach and embarrass the heart, besides, the state of emptiness of the stomach throughout the rest of the day will allow gas to accumulate in the stomach

Gas-forming foods, such as potatoes, cabbages, sprouts, cauliflower, cucumbers, turnips, bread, cakes and pastry, cheese and effervescent drinks, should be avoided as they lead to gastric distension

Indigestible and hard foods, such as onions, spices, gravies, condiments, salmon and shell fish, should be stopped, as powers of digestion are impaired in such cases

The co-existence of other diseases or complications should be taken into consideration, this is specially so in the case of kidneys disease. When cardiac and renal failure are both present adjustment of the dietary becomes difficult owing to the existence of contradictory factors

The state of nutrition of the patient requires attention. Obese patients with heart disease are frequently benefited by measures aimed at reducing the weight of the patient, low calorie diets are of value in such cases. On the other hand, in fragile and ill-nourished subjects, a fattening diet is indicated. A diet of approximately 1,000 or 1,200 calories is suitable for the average cardiac case

The diet should receive attention from the qualitative aspect also. Proteins and fats should be given in moderation, carbohydrates being a good source of energy and readily assimilable, should be given in sufficient amounts to make up the calorie-value of the diet. A restriction is advisable in the intake of sodium chloride, the sodium ion has been shown to be of greater importance than the chloride ion in the retention of tissue-fluid. The diet should contain adequate amounts of vitamins, especially vitamins B and C

Change of habits—Since attacks of paroxysmal dyspnoea occur mostly at night time the following measures may serve to prevent attacks

Taking of a sedative medicinal preparation at bed-time. Phenobarbital may suitably be combined with a purine diuretic for this purpose

A light supper taken early in the evening, with little to drink

The patient's head should be kept propped up with pillows, during the night

Digitalis—The use of digitalis has been objected to, in cases of left-sided failure, on the grounds that it raises the blood pressure with deleterious effects. This is true of digitalis in large doses, as administered to animals, but in therapeutic doses, as used in man, digitalis has no pressor action at all, if anything, there may be a slight reduction in blood pressure (Fishburg). In order to decide this moot point, the following investigation was undertaken

Frequent estimations of the systolic blood pressure were carried out in 25 cases of left-sided failure (secondary to essential hypertension), before, during and after digitalis therapy. 15 minims of the standardized tincture of digitalis (or two pink granules of Nativelle's

Digitaline) were given three times daily in these cases. From the results of the investigation, it was apparent that digitalis, at least in moderate dosage as used in man, has no constant effect on the systolic blood pressure. There is no constant rise or fall of blood pressure during or after digitalis medication.

In recent years, the use of digitalis has been urged in cases of left ventricular failure by Harrison, Fishburg, Parkinson and others. They claim excellent results from the use of this drug. Digitalis and allied preparations when used in cases of left-sided failure do seem to relieve the dyspnoea to some extent and cause an all-round improvement in the general condition of the patient. If the patient with left-sided failure can tolerate digitalis, there is no harm in continuing the administration in small doses even for years. I am in the habit of giving one pink granule of Nativelle's Digitaline (gr $\frac{1}{40}$) which corresponds to about 7 minims of tincture digitalis, three times a day for long periods of time. From the physiological point of view three granules of digitaline a day may appear too insignificant a dose but as long as the clinical results are promising, such a dosage is worth trying. After all, the value of a medicinal preparation is to be judged in terms of clinical results and not in terms of animal experiments!

Javey and Parkinson found digitalis administration beneficial in both forms of cardiac failure, viz failure with normal and failure with abnormal rhythm. Better results were obtained, by these workers, in cases with a rheumatic aetiology. The *mode of action* of digitalis in cardiac failure with normal rhythm (e.g. in left-sided failure) has repeatedly been the subject of speculation in medical circles. The subject has recently been re-opened by Paul Wood who finds our present-day conceptions on the subject unsatisfactory.

The beneficial action of digitalis has been attributed to vagal slowing of the heart, with corresponding increase in the diastolic rest-period of the heart. This is disproved by the fact that digitalis causes a fall of venous pressure in all such cases, irrespective of whether the heart-rate is affected or not.

According to Dock and Tainter, digitalis is useful in these cases because it acts like a "bloodless venesection". By causing constriction of the hepatic veins, it dams back blood in the liver and spleen. If this explanation were true, one would expect an enlargement in size of the liver and spleen in cases deriving benefit from digitalis. Clinical observation is opposed to such a view, there being a shrinking rather than enlargement of the liver, after digitalis. In cases of left-sided failure with enlarged and tender liver, that I have been able to observe, digitalis has been instrumental in relieving both the dyspnoea and the pain and tenderness in the right hypochondriac region, a diminution in the size of the liver has also been apparent. In a few cases of this type, a diminution in the size of the liver has been observed even when the dyspnoea has been completely uninfluenced by digitalis. It has been convincingly demonstrated of late by Paul Wood, with the use of thorotrast and x-ray visualization of the liver, that the liver, in cases of failure with normal rhythm shrink-

in size after digitalis therapy

There is, however, one type of case that seems to do badly on digitalis. Some patients, the subjects of coronary arterio-sclerosis, who have been subject to attacks of angina or coronary thrombosis are quite intolerant of digitalis, even when administered in small amounts. These cases get severe attacks of angina or heart-pain as the result of digitalis administration. I have, under observation, at present, a Parsi lady, with left-sided failure (of hypertensive origin) and a past history of coronary thrombosis, who tends to get severe attacks of chest-pain even on five or ten minims of digitalis tincture. Whether such pain from digitalis is secondary to coronary spasm or to increased functional capacity of the heart, it is difficult to say.

Diuretics—Diuretic substances, both purine and mercurial, are useful in cases of left ventricular failure and may serve to avert impending attacks of acute or subacute pulmonary oedema. Amongst mercurial diuretics, the most used at the present day are Novurit, Salyrgan, Neptal, Esidrene, Mersalyl and Diurin. Provided they are used with caution, they are much more effective than purine diuretics. I find the following scheme useful in cases of left-sided failure. A diuretic preparation like Deriphyllin (Homburg) in doses of 10 drops two or three times a day, or tablets of Aminophyllin, Inophylline (Milot) or Calcium-Diuretin (Knoll) one tablet two or three times a day, is kept up for long periods of time. When the pulmonary congestion is increasing, as shown by increasing dyspnoea or crepitations, an intravenous injection of 2 ccs of mercurial diuretic may prove of value in prevention of impending attacks of pulmonary oedema. The injection may be repeated at intervals of two to four days if found necessary, provided there is no impairment of renal function.

Recently, a new form of treatment has been advocated in these cases. A "pulmonary plus-pressure machine", devised by Plesch, has given good results in the hands of Poulton and others. In attacks of cardiac asthma, considerable relief has been noted within a few minutes, with the use of this clever mechanical device. A "blower" supplies air under pressure to a face mask. With the aid of manometer a positive pressure of about six inches is usually maintained. A machine of this type can be improvised quite simply from an ordinary vacuum-cleaner, used for household purposes.

Treatment of Acute Pulmonary Oedema

This condition should be regarded as a medical emergency and treated promptly with heroic measures.

The first essential is to give morphia. Some prefer to give more expensive proprietary preparations like Omnopon and Dilaudid, which possess no special merits. The morphine treatment of exudative pulmonary congestion, we owe to the late Sir Clifford Allbutt. The dramatic effect of morphine in these cases has not been adequately explained. It has been attributed by some to decrease in the venous return to the heart, Boyd and Scherf attribute the beneficial action of morphine to a depressed sensitivity of the respiratory and other centres in the medulla.

In cases of severe congestion of the lungs, even in the absence of acute pulmonary oedema, morphia may help. For this purpose morphine sulphate in doses of $1/10$ to $1/8$ of a grain, two or three times a day is recommended.

It is a customary and wise precaution to inject atropine sulphate grain $1/50$ to $1/100$ with the morphia. East and Bain recommend an injection of $1/50$ grain of atropine sulphate about a quarter of an hour before the injection of morphia, on theoretical grounds, in practice, however, no particular advantage is apparent after the adoption of this procedure. It is a popular notion that atropine is beneficial in cases of acute pulmonary oedema on account of its inherent property of drying up secretions, this is very unlikely in pulmonary oedema, where fluid accumulations in the lung are of the nature of a passive transudate and not exudate or secretion. Atropine probably acts beneficially in these cases by reducing the super-added spasm and turgescence, of the walls of the bronchioles.

Venesection is frequently, beneficial in cases of acute pulmonary oedema. Venesection or phlebotomy is a useful therapeutic measure, of value not only in systemic engorgement but also in cases of isolated left-sided failure with pulmonary engorgement, in such cases, there is a prompt relief of symptoms like dyspnoea and orthopnoea, while fluoroscopy demonstrates a "clearing" of previously congested or passively hyperaemic lung-fields. The mode of action of venesection in such cases has not, so far, been adequately explained. It is no use removing blood with hypodermic syringe and fine-bore needle, as is the practice of some physicians, in order to be effective therapeutically, venesection needs to be done within as short a time as possible, the blood is either withdrawn with a wide-bore French reedle or allowed to flow out for some time after incising the anti-cubital vein with a scalpel. There are no fixed rules about the amount of blood to be removed, as a rule, venesection should be avoided in subjects of anaemia, plethoric subjects of hypersthenic habits can afford to lose much more blood than asthenic individuals of smaller build.

Oxygen inhalation is helpful in cases of pulmonary oedema, especially when the patient is cyanosed. It is no use administering oxygen by the old-fashioned "funnel method". The most effective method of giving oxygen is by the use of an oxygen-tent or oxygen-chamber, failing this, a simple nasal catheter or better still, a forked nasal tube such as that of Marriott and Robson, may be tried. The practice of certain physicians of giving oxygen intermittently for short periods of time, e.g. administration every five or ten minutes, can only be deprecated. To derive maximum benefit of oxygen, it should be administered continuously or for long stretches of time.

Injection of 0.5 cc of adrenaline hydrochloride (1 in 1000) has been used with success in these cases by Graham, its indiscriminate use may end in tragedy. Stimulation of the heart and respiration may be necessary in bad cases of pulmonary oedema, for this purpose, Cardiazol, Coramine, and Strychnine may be used, though the pharmacological evidence in favour of their use is unsatisfactory.

(To be continued)

Reflections and Aphorisms

THE TYRANNY OF THE SICK

"The sick man's will to represent some form or other of superiority, his instinct for crooked paths, which lead to a tyranny over the healthy—where can it not be found, this *will to power* of the very weakest? The sick woman especially. No one surpasses her in refinements for ruling, oppressing, tyrannizing. The sick woman, moreover, spares nothing living, nothing dead, she grubs up again the most buried things. Look into the background of every family, of everybody, of every community, everywhere *the fight of the sick against the healthy*—a silent fight for the most part with minute poisoned powders, with pin-pricks, and with those spiteful grimaces of patience."

NIETZSCHE

THE PATIENT AND THE PHYSICIAN

"The physician should cultivate an attitude of complete objectivity which enables him to see in the irritating conduct evidence of special personality problems belonging to *the inevitable man within his patient*, and not to a vicious disobedient, and aggressive boor. But just as the man within may obstruct the healer's effect so may he as frequently, if understood, become a strong and effective ally. To maneuver him into that position is the doctor's essential task. The great physicians of the past who managed their patients successfully often possessed a better knowledge of mankind than of pathology and the basic mechanisms of disease. Indeed such medical men were generally credited with what has been halfmockingly called the good "*bedside manner*." Actually this quality rose from them as a *distillate of objectivity, intuition, common sense, and good manners*. These virtues combined with high powers of observation resulted in the superior value of such men in medicine. Nevertheless, when one considers the actual paucity of knowledge at that earlier time, it is remarkable how much those *medical biologists* were able to achieve in the relief of symptoms and in the rehabilitation of their patients. Beyond this, they likewise handed on to their successors many clinical observations and correlations which later became the basis of contemporary medical research.

The relationship between patient and physician, as in all other forms of human contact, trembles in the balance at the outset. Its nature may be established for better or for worse at the first glimpse. Ordinarily the physician has the advantage. For at least until the patient is able to discover a weak spot in the doctor's supposedly complete armour of knowledge, skill, and experience, the latter is in the power position. The patient is the suppliant who brings a *tortured body* and a *heart filled with fear*. The physician's first concern, therefore, is *to dispel the latter and in its place to establish confidence*. If the doctor succeeds in fixing within the patient's mind the concept, "*he understands me*," he will have made the first knock on that door of the patient's private chamber wherein is deposited a large part of the evidence for diagnosis and possible cure."

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Original Contributions

CIRCULATORY FAILURE AND ITS TREATMENT

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(Continued from page 251)

For *Cheyne-Stokes breathing*, the following measures are recommended. Their beneficial action is however temporary and fails to remove the root-cause of the condition. Vogl's treatment. This consists in giving intravenous injections of aminophyllin or euphyllin, in 0.24 g doses, and inhalation of carbon dioxide gas.

Right-sided cardiac failure

Failure of the right side of the heart may be primary or secondary to left-sided failure.

The *primary type* of right-sided failure usually occurs in diseases of the lungs and pulmonary blood-vessels, where there is increased resistance in the pulmonary circuit. Common examples are

Diseases of the lungs, e.g. emphysema, fibrosis and pneumoconiosis, pulmonary artery diseases, e.g. pulmonary endarteritis, severe grades of kypho-scoliosis. Heart failure is said to account for 60 per cent of the deaths in cases of severe kypho-scoliosis. Several factors are concerned in the genesis of heart failure in such cases, e.g. kinking of main blood-vessels, atelectatic areas or areas of collapse in the lungs, chronic inflammation of the bronchi etc. Diseases of the pulmonary and tricuspid valves, and an acute form of right-sided failure is sometimes met with in cases of pneumonia and in pulmonary embolism.

The *secondary type* of right side failure arises as a sequel of left-sided failure e.g. in hypertensives. The exact mode of production of right-sided failure in such cases has not been satisfactorily explained.

Clinical features—Main features to note in the clinical picture of right-sided cardiac failure are

Cyanosis is frequently observed, (in left-sided failure cyanosis is unusual), dyspnoea occurs but is, as a rule, less intense than in cases of left-sided failure, engorgement of veins with visible pulsation, the latter feature is not constant. Lewis has described a useful sign for detecting venous engorgement in such cases. The venous pressure shows a characteristic rise, it may be as high as 30 mms of water or more, enlargement of the liver with tenderness in the right hypo-

chondrium The liver shows pulsation of an expansile nature in cases of tricuspid regurgitation, manual pressure on the liver frequently causes distension of the jugular veins, in cases of congestive cardiac failure (hepato-jugular reflex of William Pasteur) Though icterus is rare, in cases of cardiac failure, a mild degree of latent jaundice, as demonstrated by a rise of bilirubin-content in the blood, is not infrequently encountered Splenomegaly, which is rarely associated with cardiac failure in European countries, is common enough in India to attract notice

Oedema is practically constant It is usually confined to the lower extremities in ambulant patients and forms sacral and trochanteric pads in recumbent cases Oedema of the face and upper extremities developing in cases of cardiac failure should suggest one of the following possibilities an extreme degree of decompensation of the heart in such cases, the prognosis is necessarily grave, oedema from associated kidney-failure, development of pericardial effusion, in several cases of congestive cardiac failure with large hearts, my attention has been drawn to the pericardial sac by a development of oedema in the face and hands, exploration of the pericardial sac with a fine-bore needle in such cases has usually been rewarded by the discovery of a pericardial effusion Unilateral oedema of one upper extremity is often due to some odd posture the patient assumes during sleep, the habit some cardiac patients display of sleeping with one arm hanging down the side of the bed is not infrequently responsible for the development of oedema in that arm, another posture that predisposes to unilateral oedema is sleeping with one arm twisted under the head

Ascites and hydrothorax are common French clinicians have described, under the designation of "asystole hepatique" a form of cardiac insufficiency with hepatomegaly and recurrent ascites as predominant features Why peripheral oedema should take the upper hand in some cases of congestive failure and ascites in others has not been adequately explained It is perhaps true to say that in the majority of cases of right-sided failure, peripheral oedema precedes ascites In cases where ascites ante-dates peripheral oedema, there is usually some associated abnormality or factor that induces this reversal of the normal sequence of events association of liver disease, portal, multilobular cirrhosis may be associated with cardiac failure, the entity generally known as "cardiac cirrhosis" is, however, rarely encountered Unhealthy state of the peritonium, Megaw stresses the frequency of "post-dysenteric ascites" in India, improper handling of bacillary dysentery cases results in spread of toxins to the peritonium with resulting "irritative peritonitis" Mediastino-pericarditis Miscellaneous causes, in the absence of associated disease, the ascites of cardiac failure usually owes its inception to a combination of factors
 1 Rise of hydrostatic pressure inside the capillaries of the peritonium
 2 Increased permeability of capillaries
 3 Portal congestion
 4 Obstruction to lymph-flow from the thoracic duct, due to rise of venous pressure
 5 Lymphagogue action of toxins on vessel walls these toxins are produced in excess because of an unhealthy or congested gastro-intestinal tract and are not properly destroyed by the

cardiac liver 6 A fall of plasma proteins, from loss of albumin in the urine

Hydrothorax, or transudation of fluid into pleural sacs, may constitute the first sign of right-sided failure. Its discovery is often accidental, during routine examination of the patient. According to Steele, cardiac hydrothorax shows a predilection for the right pleural sac especially in cases of right-sided failure. Many different hypotheses have been put forward to explain this right-sided incidence in the case of cardiac hydrothorax, (1) Looping of the vena azygos major vein around the hilum of the right lung, owing to increase in weight of the enlarged heart (Bacell) (2) Compression of pulmonary veins on the right side by an enlarged right auricle (Fetterolf and Norris) (3) Tendency on the part of cardiac cases to lie on their right side, in bed, thus predisposing to transudation on that side (4) The enlarged and congested liver of cardiac failure interferes with absorption of fluid from the right pleural sac by restricting the movements of the diaphragm

Treatment of right-sided failure

Rest physical and mental is essential. The beneficial effects of rest on the heart are probably due to a combination of factors. Decrease in the work of the heart. Exertion, physical or mental, involves increase of cardiac output and a rise of arterial blood-pressure, both these factors militate against recovery by overworking the already over-worked heart. According to Crighton Bramwell, rest promotes a gradual increase in cardiac reserve. By slowing the "tempo" or rate of the heart, rest procures an increase in the diastolic period or "rest period" of the heart.

It is important to note that under exceptional circumstances, even in cases of heart disease, complete rest in bed may be contraindicated, for example, in fully compensated cardiac insufficiency, complete or absolute rest in bed may do more harm than good, in these cases, a regime advocating "periodic rest" and "graduated exercise" is more suitable.

Many different types of bedsteads are available for nursing cardiac cases, e.g. Lewis's bedstead, Sister Rawson's heart table, etc.

The value of undernutrition in heart cases is not sufficiently appreciated by the profession. A reduction in the calorie intake to 800 or 1200 calories per day, for a few days may give great relief to the patient's heart, the work of the heart is reduced by a lowering of the oxygen consumption of the body. A low-calorie diet must however be well-balanced.

Restriction of fluids and salt is beneficial in cases with oedema or high blood pressure, an indiscriminate application of this measure to all cases of cardiac failure or weakness without a consideration of the state of the renal parenchyma, is to be deprecated. Starchy foods, by promoting formation of gas in the stomach and intestines, may embarrass the heart. High carbohydrate diets have recently been advocated by Shirley Smith and others in the treatment of heart failure.

Digitalis is perhaps the remedy par excellence in cases of this kind. Since the time of Withering, that is for a period of one hundred and fifty years, digitalis has held an unrivalled reputation in the treatment of heart disease.

The mode of action of digitalis is highly complex and not clearly understood. Cushney has written a large monograph on the subject of digitalis action on the heart. The drug appears to act on the heart in a complex manner—By stimulation of the vagus nerve, it slows down the pace-maker of the heart, depresses the conductivity of the conducting tissues in the heart and shortens the refractory period of auricular muscle. By direct action on conducting tissues, it depresses their conductivity. By direct action on muscle-fibres, it increases the strength of systolic contraction and prolongs the refractory period.

The main actions of digitalis on the heart may be summarized as follows—The rate of impulse formation at the S A Node is reduced, i.e., the heart is slowed. The strength of contraction of the ventricles is increased. The conductivity of the bundle of His is reduced. The tendency to ectopic beating is increased.

The beneficial action of digitalis on auricular fibrillation cannot be explained on the basis of an arrest of circus movement in the heart. It is due to a reduction in the rate of ventricular beating brought about by digitalis action on the conducting tissues. A slower ventricular rate affords a longer diastolic rest period to the heart, a longer period of nutrition to the heart-muscle and a better filling of the heart-chambers with blood.

The mode of administration of digitalis and the choice of preparation depend on the attending physician, they should be based on the indications and characteristics displayed by each individual case.

Eggleston's method or the "massive dosage" method of administering digitalis, though popular with clinicians in America, is neither applicable nor advisable in the majority of cardiac cases in India. Its aim is to bring the patient quickly under the effect of digitalis by administering the drug in heroic doses. In order to be effective, this method necessitates constant medical care, a highly trained nursing staff and a patient tolerant of high digitalis dosage, such amenities are unfortunately not available in the majority of instances.

Originally, Eggleston had proposed a "body weight method" of administering digitalis, 1 cc (15 m) of tincture digitalis or 0.1 g (1½ gr) of digitalis leaf being allowed per 10 lbs of body weight. Having found this method both inaccurate and undesirable in practice, he modified the method to some extent by fixing an arbitrary standard of digitalis dosage. He considers 15 ccs of tincture or 1.5 g of digitalis leaf as the average effective dose for an adult.

The old-fashioned method of administering digitalis in small doses, e.g. 5 minims of tincture twice or thrice a day, has nothing to recommend it. It gives a false sense of security and confers no benefit on the diseased heart.

Digitalis has given best results when administered in moderate doses. It is important, however, to realise the difference between the

therapeutic or curative dose on the one hand and the maintenance dose on the other. In cases with a rapid ventricular rate, it is advisable to give, in most cases, an initial dose of half to one drachm of tincture digitalis. This is followed by 20 minims of tincture at 6 hourly intervals, until the rate of the heart comes down to 75 or 80. The maintenance dose of digitalis varies from case to case. The "maintenance dose" of digitalis was worked out by me in a series of twenty-five cases of right sided insufficiency of the heart. The minimum dose of digitalis tincture necessary to maintain the ventricular rate at 75 per minute for long periods of time was found to vary from 5 minims three times a day to 28 minims three times a day, the daily dose of digitalis tincture varied from 15 minims to 84 minims in the twenty-five cases. The average maintenance dose worked out for whole series was 9.5 minims of tincture three times a day. In 80 per cent of the cases, the maintenance dose per day was less than 45 minims. In order to assess the relative merits of different preparations of digitalis, cases of cardiac failure were maintained for standard periods of time on each of the following proprietary preparations of digitalis: Nativelle's digitaleine granules, Digoxin tablets (B.W. & Co.) and Digifortis liquid (P.D. & Co.). Of these three, Nativelle's granules were found to represent the most convenient and the most reliable form of digitalis preparation. One pink granule of Nativelle's Digitaleine (gr 1/600) was found by clinical trial to correspond in effect to about 7 minims of the B.P. tincture. In one case, however, it proved equivalent to as many as 11 minims of tincture, this is probably due to deterioration of tincture with storage. From the point of view of potency, 6 minims of digifortis liquid were found to be equivalent in effect to 8 minims of the B.P. tincture. Digoxin was found to be the most potent of the preparations of digitalis tried, its slowing effects on the heart are rapid, marked and protracted. For that reason, it is strongly indicated in cases with rapid heart rates where early or immediate slowing of the rate is necessary. For protracted digitalization, however, (maintenance dosage), Digoxin was found inconvenient, its action on the heart was found to be rather inconstant, with the result that a constantly changing maintenance dose was necessary. Also, toxic symptoms like nausea and vomiting were more frequently encountered with Digoxin than with the other two proprietary preparations tried.

Levy has demonstrated the effectiveness of digitalis when administered by the rectal route, he suggests this mode of administration in cases which are intolerant to digitalis by mouth. The dosage need not be higher than that given orally. The calculated dose of digitalis tincture is diluted with 25 to 30 ccs (1 oz.) of normal saline or tap water and instilled into the rectum, with instructions to retain as long as possible. Because of the intensely irritating qualities of alcohol, the delicate rectal mucosa should never be subjected to an undiluted tincture of digitalis.

Symptoms of overdosage—When administering digitalis a close watch should be kept for toxic symptoms. Because of its cumulative properties, digitalis is capable of causing toxic manifestations even

in small doses provided it is administered for a sufficient length of time. Sensitivity to digitalis varies enormously from patient to patient. Toxic symptoms cannot be averted merely by combining allied preparations of digitalis or by the use of expensive proprietary preparations.

The following symptoms of digitalis intoxication should be looked for

Gastro-intestinal symptoms—Anorexia, nausea, vomiting and diarrhoea. Loss of appetite is perhaps the earliest sign of digitalis overdose. It is important to realize that in cardiac cases, vomiting may be due either to portal congestion or to digitalis intoxication, in the first case, there is urgent need for digitalis while in the second, digitalis should be stopped, the treatment for the two types of vomiting being diametrically opposed, a correct diagnosis of the cause of vomiting is essential. Time and again, one sees cases of cardiac failure with severe portal congestion, who are in urgent need of digitalis, and yet allowed to go from bad to worse by withholding digitalis on the supposition that the vomiting is due to too much digitalis. If persistent vomiting occurs in a case of cardiac failure treated on digitalis, attention should be directed to the following features in order to determine the cause of vomiting: (1) Are there other signs of digitalis intoxication? A slow heart rate, frequent ventricular extrasystoles or abnormalities of the ST intervals or T deflection in the electrocardiogram would weigh in favour of digitalis effect as cause of vomiting. The dose of digitalis administered and duration of digitalis treatment should be considered before rushing to conclusions. The question should always be raised: Has digitalis been administered long enough or in sufficiently large dosage to give rise to digitalis intoxication? (2) Are there any other signs of portal congestion or severe cardiac failure? When signs of failure are present in the absence of digitalis poisoning, digitalis can be pushed without fear. In difficult cases, electrocardiography may solve the problem of whether to withhold or to increase the dose of digitalis. The mode of production of vomiting in cases of digitalis excess has been repeatedly studied by pharmacologists, whether digitalis induces vomiting by an action on the mucosa of the stomach, on the vomiting centre in the medulla or on the nerves of the heart, is not known.

Cardiac Symptoms—Excessive slowing of the heart to below 60 or 65 per minute is an indication to stop digitalis. Frequent extrasystoles and "coupling" (pulses bigeminus) carry the same significance.

Miscellaneous Symptoms and Signs—Oliguria or reduction in the output of urine is a good sign of digitalis excess. The importance of charting the daily output of urine in cardiac cases, is not sufficiently appreciated by practitioners, it affords an index of oedema-formation, cardiac function, renal function and digitalis dosage.

Headache, vertigo, blurred or coloured vision and delirium are occasionally encountered as the result of digitalis overdosage.

Since *eosinophilia* has been described as a sign of digitalis excess by some workers, I have worked out the differential white cell count

In fifteen cases of proved digitalis intoxication. In each case, 400 white cells were counted and classified according to types. The percentage count of eosinophils ranged from 0.5 per cent to 3.5 per cent in the fifteen cases, with but one exception, in this case the count was as high as 11 per cent. The calculated average for the fifteen cases is 2.0 per cent. We cannot, therefore, regard a high eosinophil count as a constant or even a common feature of digitalis excess.

Electrocardiographic Changes—The following deviations from normal in the electrocardiogram are indicative of digitalis effect: (1) Depression of ST interval, (2) flat, iso-electric or negative T waves. These alterations have been lucidly dealt with by Cohn, Fraser and Jamieson. (3) A prolongation of the P-R interval. (4) Decreased duration of electrical systole (or QT duration) in relation to the length of the cardiac cycle. (5) Presence of extrasystoles, with tendency to "coupling" or pulses bigemini. (6) Notching or slurring of QRS complexes. (7) Inversion of P waves. The last two features are inconstant.

Contra-indications to digitalis—Defective conductivity of the Bundle of His with partial heart block is a contra-indication to the use of digitalis. This objection does not hold good in the case of complete heart block or bundle branch block. The question frequently arises: Are we justified in giving digitalis to cases of failure with frequent extra-systolic beats, since digitalis is itself a potent cause of ectopic beating? The present day teaching is that administration of digitalis is justified in such cases, provided there is definite evidence of cardiac insufficiency.

Diuretics—Diuretics have an important place in the treatment of heart failure. Two main groups of diuretics are favoured at the present time, xanthine derivatives, e.g. theobromine, theophylline, theobromine sodium salicylate (diuretin), theophylline-ethylenediamine (aminophyllin, euphyllin or inophyllin) and theobromine calcium salicylate (theocalcin). Recent work suggests that the cardio-therapeutic virtues of these preparations are due partly to their diuretic action and partly to their property of inducing a better coronary circulation. Xanthine derivatives are administered orally (e.g. 0.5 g diuretin, three times a day), intravenously (e.g. 0.24 g aminophyllin) or intramuscularly (e.g. deriphyllin, 2 c.c.s.) mercurial diuretics, e.g. salyrgan, mercuripin, novasurol, novurit, neptal, merasiyl etc., are as a rule more effective and dramatic in their results than xanthine derivatives. They remove oedema, relieve portal congestion and cause an amelioration of the dyspnoea and other symptoms.

The site of action of mercurial diuretics has not as yet been elucidated, whether the action is primarily renal or extra-renal, whether it is on glomeruli or tubules, are problems which require solution. According to Hermann and others, mercurial preparations act by inhibiting tubular re-absorption in the renal parenchyma.

Mercurial derivatives are contra-indicated in patients who are moribund and in patients with haematuria or impairment of renal function. In Fishburg's opinion, their use should be interdicted in cases where the specific gravity of urine falls below 1010 or 1015. The diuretic action of mercurials may be enhanced by the administration

of ammonium chloride, ammonium nitrate, calcium chloride or some similar acid salt 4 to 10 g of ammonium chloride are given daily, by mouth for three or four days along with, or, preceding the mercurial preparation. The latter should first be given in a small dose ($\frac{1}{2}$ c c) intramuscularly, in order to test the patient for idiosyncrasy to mercury. If the patient is tolerant of this test dose, larger doses of the preparation may be administered intravenously at intervals of three or four days, it is unwise to exceed a dose of 3 ccs at any time. Toxic symptoms of mercurial poisoning, e.g. stomatitis, colitis, fever, albuminuria, haematuria, oliguria and peripheral shock or collapse are rare, provided there is no renal insufficiency present. Care should be exercised in the selection of patients for mercurial treatment, with a renal function that is unimpaired, there is little danger of inducing toxic symptoms with mercurial diuretics.

Venesection, "bleeding" or phlebotomy—There was a time, when this therapeutic measure was employed universally for every conceivable complaint, like all measures that are enthusiastically acclaimed by the profession to begin with, phlebotomy fell into discredit for some time and was practically abandoned. At the present day, its use as a therapeutic measure is limited to certain diseased conditions and it enjoys a definite place in the treatment of heart disease.

Venesection gives excellent results in cases of systemic venous engorgement and of severe pulmonary congestion or oedema. After removal of about half a pint of blood, there is usually a striking amelioration of symptoms and a characteristic reduction in the size of the heart, the latter feature has been convincingly demonstrated, radio graphically, by Gordon, who claims to have frequently observed a reduction in the transverse diameter of the heart of 2.5 cms or more, after a single "bleeding". The beneficial effects of venesection may be explained as follows: by removing a fair quantity of blood from the venous system, the volume of blood returning to the right side of the heart is diminished, this allows the muscle-fibres of the right ventricle to shorten to a size at which they can contract most effectively.

Glucose Therapy—Intravenous administration of hypertonic glucose has been strongly recommended of late in cases of heart failure by European and American clinicians. 50 to 100 ccs of a 50 per cent solution of glucose is given once or twice daily, intravenously. Excellent results have been claimed with this measure in cases of angina pectoris, congestive cardiac failure, cardiac asthma and paroxysmal tachycardia. The mode of action of glucose in these cases is probably complex. It improves the nutritional state of the heart muscle, a failing heart is said to require more carbohydrate for its needs than a normal heart. Glucose augments the action of digitals in cardiac cases. It is also a mild diuretic.

Defects and Deficiencies of the French Classification of Cardiac Failure—Though the French classification of cardiac failure into left-sided and right-sided has been adopted in the present paper, it cannot be considered perfect or above reproach. Too much stress has been laid in this classification on isolated or "pure" forms of failure, where only one side of the heart is affected, mixed or combined forms

of failure, with affection of both sides of the heart, receive but scant attention from French authors. In actual practice, I find the isolated forms of failure accounting for a comparatively smaller number of cases than the mixed or combined forms of failure, in the majority of failure cases, encountered in clinical practice, there appears to be a participation of both chambers of the heart in the genesis of failure. In this classification of heart failure, there is no attempt at differentiation of cases with normal from those with abnormal rhythms, in spite of the great difference in prognosis and treatment of the two types.

MIXED OR COMBINED FORMS OF CARDIAC FAILURE

These may arise in one of two ways (1) Both sides of the heart may fail simultaneously as in cases of hyper- and hypo-thyroidism, anaemia, hypoglycaemia and arterio-venous fistula (2) Left sided failure, isolated to begin with, may induce failure of the right side of the heart at a later date. The reverse process is also encountered, though less frequently.

Combined failure of the heart is very common in practice. There is little or no uniformity in the clinical picture of combined failure, there being a varying assortment of symptoms and signs. Clinical features of left sided failure are intimately combined with those of failure of the right side, the relative preponderance of each chamber of the heart in its contribution to the final clinical picture, varies from case to case. Hence the extreme difficulty of classifying cases of combined failure of the heart into sub-groups. After a study of these cases, one begins to discern certain "clinical types" or "pictures" even in this strange assortment of symptoms and signs. Whether one is justified in classifying or "splitting" combined failure into further sub-divisions or groups, is open to question. For want of a better classification of combined failure, the following "grouping" of cases is provisionally suggested in an attempt at establishing some sort of order in this state of chaos.—The type of "picture" which is most frequently encountered in practice is somewhat as follows. There is dyspnoea, continuous or paroxysmal or both, basal crepitations are found on one or both sides of the chest, though more commonly on the left than on the right side, there is oedema, slight or moderate, usually limited to the ankles ("puffiness" of the ankles) and often confined to the later hours of the day, the jugular veins are moderately engorged and prominent in the neck, though actual pulsation is seldom obvious, venous pressure, as determined in the ante-cubital veins, usually lies between 9 and 18 cms of water. Though palpable enlargement of the liver is usually slight or even absent, some degree of tenderness in the right hypochondrium is practically constant. Pulsus alternans and bruit de galop are seldom met with in this group. There is no ascitis or hydrothorax, attacks of pulmonary oedema do not occur. Fluoroscopically, the hilar shadows are prominent, there is some degree of pulmonary hyperaemia of the millary, basal or peripheral type and the cardiac shadow shows a spherical, triangular or rarely a "boot shaped" configuration. Measurement of circulation rate usually reveals a prolonged "arm to tongue time"

(Magnesium sulphate method, Calcium gluconate method or Decholin method) and a normal "arm to lung time"

Bernheim's syndrome—This type of failure, though common enough in practice, especially in hypertensive subjects, is unknown to most physicians. Apart from a few scant references to this form of failure in France (Bernheim, 1910, Mazzei, 1931) and America (Fishburg), there is no mention of it in the medical literature of other countries. In Bernheim's syndrome, one observes a unique combination of signs. The hypertensive state is associated with a severe form of right-sided failure with little or no evidence to suggest insufficiency of the left ventricle, this is truly strange, considering that it is the left ventricle and not the right which is subjected to strain in cases of high blood pressure. In this syndrome, there is usually a moderate or severe degree of oedema, severe congestion of the neck-veins with or without visible pulsation, hepatomegaly with tenderness in the liver area, a few or no crepitations at the lung-bases and a normal second sound at the pulmonary area.

The combination of right side failure with hypertension, as witnessed in cases of Bernheim's syndrome, is difficult to explain. Bernheim and others, on the basis of autopsy findings, have attributed this syndrome to partial obliteration of the right ventricular chamber by a grossly hypertrophied inter-ventricular septum, such as occurs in some cases of hypertension. This "bulging" or "deviation of the septum" leads to Bernheim's syndrome by inducing the following alterations in circulatory dynamics. Since the partially obliterated right ventricle is incapable of receiving its normal or full quota of blood from the right auricle and veins, blood tends to accumulate in the vanae cavae tributaries, manifestations of right sided failure, such as are encountered in cases of Bernheim's syndrome, are attributable to this enlargement of veins. Diastolic filling of the right ventricle is impeded partly by the small size of the right ventricular chamber itself and partly by the increased pressure within the left ventricle. Because of deficient diastolic filling there is a corresponding diminution in the output of the right ventricle, the latter feature is responsible for the curious lack of pulmonary engorgement and other manifestations of left sided failure, in these cases. It is possible that some of the cases of so called Bernheim's syndrome, which fail to show septal bulging, are attributable to other causes, co-existence of left sided hypertensive failure with disease of the coronary arteries on the right side, co-existence of emphysema (with its attendant effects on the heart, the so called "emphysema heart") with left-sided hypertensive failure.

As emphasized by Fishburg, Bernheim's syndrome is most often encountered in youthful subjects of hypertension, subjects whose heart muscle fibres are capable of extreme grades of hypertrophy and "bulging"

"Asystole Hepatique"

Cases of hypertensive heart failure are occasionally seen where the main brunt of the disease seems to have fallen on the liver, the predominant sign of failure in these cases is a large and tender liver,

which may extend to even below the level of the umbilicus. Ascites, moderate or severe, is frequently associated with the hepatomegaly. Enlargement of the spleen may be observed in the later stages of the failure. This condition is liable to be mistaken for "cirrhotic liver with ascitis" or Banti's disease. In order to direct attention to its most striking feature hepatomegaly, the condition has aptly been referred to, by French clinicians, as *asystole hepatique*. The association of this type of heart failure with high blood pressure is difficult to explain. Though signs of pulmonary congestion appear to be strangely lacking in this condition, careful examination will practically always disclose the presence of crepitations at one or both lung bases, in other words, left sided failure is present but in a latent form.

Enlargement of the liver may occur in these cases with no engorgement of veins or elevation of venous pressure, such an association of signs is decidedly unusual in cases of heart failure, except in the mildest of cases. Since the hepatic veins open into the inferior vena cava quite close to the right auricle, there is every good reason why palpable hepatomegaly should be one of the earliest manifestations of right-sided failure, in the opinion of Fishburg, liver congestion occurs earlier in right ventricular failure than engorgement of veins or rise of venous pressure.

PERICARDITIC FORM OF FAILURE

Some cases of hypertension with decompensation display a characteristic type of clinical picture which bears a close resemblance to the clinical entity recently described by Paul White and others under the designation of *chronic constrictive pericarditis*. The main features to note in such a case are Tender and palpable enlargement of the liver, a rapidly recurring ascites, a severe degree of venous engorgement with the jugular veins prominent and pulsating, oedema of the ankles or legs, a normal or practically normal arterial blood pressure. It is a point, worthy of note in connection with hypertensive heart disease, that a previously high pressure may fall to normal levels when failure of the heart sets in.

This form of failure may be recognised from chronic constrictive pericarditis by a consideration of the following points: the size of the heart, in constrictive pericarditis, the heart is normal in size. In constrictive pericarditis, there is no history of high blood pressure, past or present. Fluoroscopic examination of the heart in cases of chronic pericarditis reveals slow and sluggish movements of the cardiac borders and evidences of calcification of the pericardium.

Miscellaneous forms of failure—There are cases of "Mixed failure" of the heart, encountered in practice, which do not belong to any of the above-mentioned groups, this is a heterogeneous collection of cases, with widely different symptoms and signs, all gradations being seen between isolated left sided failure on the one hand and isolated right sided failure on the other.

PENICILLIN THERAPY IN SYPHILIS

A REPORT ON 21 CASES

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The experiments with penicillin of Mahoney and his associates in 1943 opened up a new era in the treatment of syphilis. Spirochaetes were proved to diminish in numbers and disappear from open lesions, skin lesions healed and the blood serology was reversed or showed a tendency to reversal by the use of the new drug. Various techniques were employed to try and determine an optimum time dose relationship. Although small and large doses gave similar immediate results, it became obvious with time that the incidence of relapse was in inverse proportion to the quantity of the drug injected.

The total dosage chosen in our series was usually of 24 millions O.U. In some cases a total of only 12 millions was given for economic reasons. It was administered mainly in two variations, viz, 40,000 O.U. three hourly and 20,000 O.U. three hourly by intramuscular injection. The initial dosage, with a view to avoiding Hehrer effects, was kept low in certain cases, e.g., late syphilis. It must be made clear that this dosage is purely arbitrary and it will take years before the question of adequate dosage is settled. A similar state of affairs existed with the older methods of treatment, until the League of Nations Health Organisation, commenced in 1928, a gathering of data from various institutions in different countries and in 1935 defined definite standards for treatment. Probably it will come to the same thing with Penicillin and a general pooling of knowledge, gained from experience with this drug, over several years to come, will help us to evaluate what is the optimum time-dose relationship. Penicillin Panels to report on early cases and on late cases have been formed in America, thirty-one hospitals and the Army, Navy and Public Health Services are participating.

The only standard for gauging the efficacy of penicillin in syphilis at present, is by the incidence of serological or clinical relapse. Experience up to the present, shows that the earlier the case comes up for treatment the better the prognosis. The bigger the dose in the early stages, the better the results. Slow absorption, i.e., intra-muscular route, causes a smaller number of relapses than rapid absorption, i.e., by the intravenous route. Penicillin plus Mapharside given as follows—viz, 50 intra-muscular injections at three hour intervals of only 5,000 units each of penicillin in conjunction with 0.04 Gm of Mapharside daily, for eight days has given in a series of cases treated by the Penicillin Panel, optimum results. There was no relapse during the period of observation of 48 weeks. Either drug given individually in this dosage, would be considered as under-treatment, but given together they appear to exert a synergistic action in this disease.

A paper read at the 60th Meeting of the Seth G. S. Medical College and K. E. M. Hospital Staff Society, Bombay, on 8th June 1946 with Dr A. C. Rebello in the chair.

The Panel also report that cases resistant to As-Bi therapy react favourably to Penicillin. One case in our series had a very persistent nodulo-ulcerative or gummatous syphillide. He was intolerant to arsenic and had had a large number—over thirty—injections of bismuth combined with iodides. The rash refused to subside and we decided to try penicillin. Unfortunately, he could not afford the full 2,400,000 units and we put him on 20,000 units three hourly to a total of 1,200,000 units. After 400,000 units he showed improvement and before the end of his treatment his skin lesions had completely resolved. He was so pleased with results that he made a determined effort to raise more funds, and purchased another twelve bulbs, thus having his full 2,400,000 units. Unfortunately he has not come up for a "follow up", but we were assured, by his physicians, that there was no evidence of cutaneous relapse nearly six months after cessation of treatment. Gummata of skin, mucous membrane, and bone heal quickly under Penicillin Therapy.

Herewith is reported a summary of results following treatment with Penicillin in the Skin and Venereal department of the K E M Hospital, in 21 cases of Syphilis in various stages between June 1945 and May 1946. Included in this series is one case from the medical ward. Of these 21 cases, 12 were males and 9 females.

The following table gives the information regarding the presenting stage of syphilis of the patients as well as their serologic condition when they came up for treatment. The stages of syphilis are calculated arbitrarily on the time lapsed from the date of infection. The patients included in the primary stages are those who came up with a genital ulcer which was dark ground positive, those in the early secondary stage had a Kahn ++++ and other evidences of secondary syphilis, and up to six months from the date of infection, those in the late secondary stage had an infection which was from 6 months to 2 years old, the tertiary grouping includes the cases beyond the two years limit.

TABLE 1
Cases Classified according to the Stage & Serology

Stage	Sero nega tive	KT O or I	or WR O or I	Sero- posi tive	KT or WR 3 or 4 +	Doubt ful	KT — or — 2 2	WR	Total
1 Primary	2			1		0			3
2 Early secondary (upto 6 months)	0			2		0			2
3 Late secondary (6 months to 2 years old infection)									
Asymptomatic (Latent)	3			0		1			4
Symptomatic (Manifest)	2			3		0			5
4 Tertiary (after 2 years)									
Asymptomatic	—			0		0			—
Symptomatic	0			3		0			3
5 Congenital	0			2		0			2
	5			11		1			21

Blood Serology—Penicillin in dosage of 300,000 units, reduces the strength of the serologic reaction in the majority of cases.

Higher doses have a more marked effect. Complement-fixation tests and flocculation tests are equally affected, and the spinal fluid improves with the blood serologic reaction. In those cases where the blood serology does not alter symptomatic improvement is always noted. Higher titres show a better response. In late syphilis there is a reduction of syphilitic reagin titre in the blood in 50 to 60 per cent of cases. This sometimes follows an initial rise. If the serological titre rises at any time consistently, after a previous decline, it is probably a sign of relapse. On the whole it can be said that the serological reaction with penicillin is very much the same as with As and Bi treatment.

In our series only four out of the eleven sero-positive cases are available for final analysis, and all four are sero-negative now. One case which was serologically doubtful to start with, is negative now. Out of the nine sero-negative cases treated, six are available for final analysis, and all six are sero-negative up to date. Out of the latter group one case of late syphilis with optic atrophy, showed a Herxheimer serologic response—the blood reaction becoming strongly positive during and immediately after treatment. Now again the blood has returned to normal.

Primary Syphilis—There were three cases of primary syphilis out of which one was sero-positive, and two sero-negative as well as dark-ground negative due to previous treatment. The clinical response to treatment was good in all these cases, the primary ulcer healing in eight to ten days' time. Complete 'follow up' is available in only one case, who is still clinically and serologically negative. One case has not come to us for a subsequent check up. The third case finished his treatment only a week back and it is too early to report on him.

Early Secondary Syphilis—Three cases of sero-positive early secondary syphilis are reported, all of whom responded clinically well to treatment. The rash commenced subsiding in four days, and had completely subsided in seven to eight days' time. One case, that of a pregnant woman, is reported fully below, another case has not seen us for a "follow up". A third case saw us only recently. Clinically she has improved considerably and only a residual pigmentation marks the site of her former eruption. On admission cervical and urethral smears were positive for gonococci in the third case, and these were negative at the conclusion of treatment. Both the cases which have come for a "follow up" are serologically negative, six months after treatment was instituted.

Pregnancy—Favourable reports have been received in the treatment of pregnant women with Penicillin. The drug has been proved to cross the placental barrier by its demonstration in the umbilical vein of the newly-born infant, following its use in the mother, immediately before parturition. In the majority of cases, the child is apparently born healthy and clinically and serologically the mother and child appear to show a favourable response. Some cases tend to relapse following child birth. There is always a small but possible danger of abortion, from a Herxheimer response at the diseased placental site, and caution with initial dosage is imperative.

One case of a woman five months pregnant was treated by us. She had an extensive florid eruption and all the symptoms of early secondary syphilis. She was given 20,000 units 3 hourly for the first 1,200,000 units to avoid a Herxheimer reaction and 40,000 units every three hours for the next 1,200,000 units. She remained sero-positive, although clinically she was "cured" at the end of treatment. There was no tendency to sero-reversal for the next two and a half months, and in the interest of safety for the child, it was decided to start her on a course of mapharside and bismuth. She took in all 0.22 Gm of mapharside and 0.4 Gm of bismuth before delivery. At birth the child weighed 6½ lbs and was apparently healthy. At 2½ months which was the last period of observation, there were no evidences of disease. Both mother and child at this period were clinically and serologically normal. X-rays of the long bones of the child showed no evidence of osteo-chondritis. Sero-reversal is expected with penicillin between twenty and seventy days. A patient with a strong positive reaction after 90 days should, according to present standards, have further treatment.

Congenital Syphilis—In congenital syphilis again, the reports are favourable. Penicillin having very little toxicity, is the drug of choice in the treatment of syphilitic infants, who are always a poor risk. The only caution necessary is in the avoidance of Herxheimer response in an unhealthy and weakly patient, whose body resistance is not developed and whose tissues are teeming with Spirochaetes. Epiphyseal and bone lesions have shown improvement under penicillin treatment.

We have treated two cases with a total dosage of 20,000 units per kilo body-weight. The dosage on the first day was 5 per cent of the total dosage, on the second day 10 per cent and on the subsequent days 15 per cent. Injections were given intramuscularly throughout the 24 hours, at the usual three hourly intervals. One of the cases developed epileptiform convulsions involving the left extremities, on the third day of treatment. These were checked by bromides and chloral hydrate, penicillin being continued throughout. This emphasises the necessity for caution as mentioned above. Both the cases responded well clinically. The surface lesions healed at the termination of treatment. There were no other clinical signs of syphilis. The other case developed a diffuse, follicular itching eruption on the ninth day of treatment which persisted when the patient was discharged, this rash subsided gradually after six weeks. Only a calamine lotion was prescribed. The patient came up for re-examination one week ago, i.e., three months after conclusion of treatment. The child is clinically and serologically normal. The problem of whether the dosage given is adequate, remains to be solved.

The C S F—The drug is not excreted in quantity in the spinal fluid, but abnormal fluids tend to improve in a large percentage of cases of late neurosyphilis. A drop in the cell count and total protein, an improvement in W R and Colloidal tests may be found early in the majority of cases. The decline may continue for some months after treatment has been stopped. If there is a rise in pro-

tein and cell count, it is a warning of relapse. Improvement has been noted in cases where As-Bi have failed. It is possible that if the spinal fluid fails to respond favourably, or after an initial response either deteriorates or shows no change, further penicillin therapy is indicated. The effect may be enhanced by a course of fever therapy.

The following table summarises the C S F findings and blood serology of the cases examined for co-relation.

TABLE 2
C S F findings of Cases examined

Case No	Normal finding in Cytology & Protein	Abnormal and/or protein and/or globulins	C S F W R	Blood W R or Kahn
1	✓		WR/O	KT/2 WR/2
2		Pr 0.08% Gl increased	WR/O	KT/3 WR/2
3	✓			KT/O
4	✓		WR/O	KT/O
5		Pr 0.08% Gl increased Cells 10 Lymphocytes	WR/O Range Normal	KT/O WR/4
10	✓		(Before Tt) WR/4 5.1-46 (After Tt) WR/2 23.1-46 (After Tt) WR/O 0.2-46 (After Tt) WR/O 29-4-46	KT 0 WR/O
12	✓		WR/O	WR/4 KT/3
14		Pr 0.1% Globulin ✓ Cells 2 Lymph	WR/O	WR/O KT/O
15		Pr 0.0% Gl ✓ Cytology	WR/O	WR/O KT 0
17	✓		WR/O	WR/O
18		Pr 0.08% Globulin ✓	WR/O	KT/O WR/O
21		7.2-46 240 Cells Lymph Protein 0.1% Gl increased	WR 4	KT/4
		22.2-46 40 Cells Lympho Pr Gl Increased	Anti Complimentary	
		8.3-46 12 Cells Lympho Pr 0.1% Gl Increased	Anti Complimentary	KT 4
		13.3-46 24 Cells Lympho Protein 0.2% Gl Incr	WR 4	

In six cases out of a total of twelve examined, the proteins were increased. In only three however was there a simultaneous increase in globulins, which alone is significant in the diagnosis of neurosyphilis. Two of these cases show also an associated increase in the number of lymphocytes. The W.R. of the C.S.F. was positive in only two cases, and in one of these the routine C.S.F. examination was quite normal. The W.R. of the C.S.F. returned to normal in one case and in unfortunately unavailable in the remaining case.

These results demonstrate the importance of complete C.S.F. examinations of all cases as any one, or all the findings may be indicative of neuro-syphilis

Neuro-syphilis—The Penicillin Panel have reported no neuro-recurrences Although it is early to make a definite statement, compared with As and Bi, results for the present have been excellent and early cases have responded particularly well Herxheimer effects such as convulsions and symptoms of myelitis have been observed and call for smaller initial dosage Improvement has been noted in varying degrees, in 80 per cent of simple demented paresis, in deteriorated paresis to a smaller extent In Tabes Dorsalis also improvement is noted and lightning pains disappeared in two patients out of seven, and was lessened in the remainder, only one case failing to respond In meningo-vascular neuro-syphilis 40 per cent improved considerably

We have treated four cases of neuro-syphilis in our series, our findings and results are summarised in Table No III

TABLE 3
Cases of Neurosyphilis

Diagnosis	Case No 3 Optic Atrophy	Case No 9 Optic Atrophy	VII Neuritis VIII	Meningo myelitis
Neurological Abnormalities	Bilateral Contraction of Visual fields more on temporal side	Same as No 3	1 Bilateral nerve type of deafness 2 Infratemporal VII N pain	1 Weakness (paresis) 2 Bladder & rectal incontinence, 3 Sensory changes
Clinical	No change None after treatment	No change	No change	1 Weakness cured 2 Visceral reflexes Normal 3 Sensation improved
Response to treatment CSF before treatment	WR/0 Pro 0.08%	Pr 0.1% WR/0 GI Increased 16 cells Lym phocytes	Routine/N.A.D WR/4 WR/4	240 Cells Lympho Pro 0.1% GI Increased WR/4
CSF after treatment	? GI Increased	?	Routine/N.A.D WR/0	24 Cells Lympho Pr 0.2% GI Increased WR/4
Remarks	No Clinical Change	No Clinical Change.	Serological spinal fluid Reversal No clinical change	Marked clinical and Cytological improvement No change in C.S.F.W.R

It emphasises that penicillin is most effective in meningo-vascular syphilis, where there is no structural abnormality It has got a definite effect on the C.S.F. cytology and WR reaction, tending to a reversal to normal Penicillin will not however perform the impossible and cannot restore structural damage, or resolve scars Of these four cases two had optic atrophy, and one had neuritis of the seventh and eighth nerves These cases did not improve clinically although one did improve serologically The fourth case was of meningo-vascular syphilis with paresis and bladder symptoms, which disappeared after treatment At first there may be a disparity between clinical improvement and laboratory findings,

the former far exceeding the latter. Abnormal C S F's show gradual reversal for some days after penicillin has been stopped. The two cases of optic atrophy showed no improvement in visual fields immediately after the treatment was terminated. These cases have not reported for check up and the final outcome is unknown. Incidentally, it should be mentioned here, that both these cases were first suspected only on examination of their fundi, fields of vision, and CSF. The patients never complained of any symptom. This emphasises the necessity for a thorough clinical and laboratory examination.

Late and latent syphilis - Within the first four years of infection, or early period of latency, therapy similar to that given in primary and early secondary cases would be expected to produce good results. In late latency however several years of treatment and observation will be required to furnish us with data on which to base treatment. Stokes advises caution, and the avoidance of too energetic treatment as in early latency. Bigger dosage, up to 4,000,000 units divided up into a series of courses rather than in one course. Fever therapy may be a beneficial adjunct as may also the use of one of the heavy metals. Almost every patient in late latency provides an individual problem. In this group we have included the remaining seven cases who, according to our classification were in the late secondary or early tertiary stage. This group comprises cases—manifest as well as latent. Some had had sub-curative As-Bi therapy, and others were intolerant to arsenic. The response to treatment is difficult to assess in these cases, as due to their partial treatment clinical and serological findings were negative before penicillin therapy was commenced. Four of these cases are still clinically and serologically normal at the time of reporting. Partially treated cases of this nature are bound to occur frequently in this uncertain period of transition from the older to the newer methods of treatment.

Visceral Syphilis — There was one case of clinically suspected syphilitic gastritis, which we report because of its interest and comparative rarity, and also because of the good therapeutic results obtained. This patient contracted syphilis thirteen years ago. He was admitted as an emergency on the surgical side, for acute pain in the epigastrium. On investigation a barium meal screening of the stomach, showed prominent rugae. The radiological diagnosis was gastritis. His blood Kahn was +++ and on the strength of this report he was transferred to us for opinion. His pain was still persistent although it had diminished and bore no relation to food. He complained of loss of weight. Further investigation revealed hypochlorhydria, microcytic anemia and WR +++ Kahn ++++. The patient could not afford penicillin and was put on small doses of As and Bi. He proved intolerant to arsenic and progressively lost weight. The advisability of trying penicillin was again put to him and he was able to purchase 1,200,000 units which were given to him in three-hourly dosage of 20,000 units each. Subjective and objective response to treatment was very satisfactory. The patient now has no pain at all, has put on 12 lbs in weight,

and is serologically negative, four months after completing his course. The latest X-ray plate shows improvement in as much as the stomach outline is returning to normal and rugae are less prominent. He is having liver and iron as supportive treatment and further progress is being watched. If progress should come to a standstill we hope to give further penicillin treatment. It should be stressed here that in cases of this type of long duration, permanent damage, e.g., fibrosis is likely to have occurred and will not respond to penicillin therapy.

Reactions to Penicillin

(1) *Herxheimer Reactions*—These have been reported as of frequent occurrence in all stages of the disease. In the primary stage quite frequently the sore becomes swollen and painful and the associated lymph glands tender, soon after treatment is begun. This is very temporary and healing is rapid. In the secondary stage the rash may become more pronounced and such symptoms as joint pains, headache, fever, may increase within the first of 24 to 48 hours, but rapidly subside after that. Such reactions are of particular importance in the treatment of syphilis in the newly born, in the later months of pregnancy, and in late syphilis with cardiovascular or cerebral involvement. These reactions can be obviated by a lower initial dosage.

In our series of cases Herxheimer reaction was observed in three cases, two of which exhibited only fever for the first 24 hours of treatment. It subsided without discontinuing treatment. The third case had both fever and an aggravation of the eruption.

(2) *Toxic Effects*—To some extent these may be influenced by impurities in the preparation and these are being overcome by newer and better methods of production. On the whole, penicillin compares extremely favourably with the older drugs used and can be given to patients where one would hesitate to use As or Bi. Mild chills accompanied by fever in some cases, severe pain at the site of the intravenous injection, cramps in the muscles, tingling in the testes, headache, flushing of the face, a moderate rise in eosinophiles, these are the accompaniments in some cases treated with drug.

In one case in our series, there was vomiting, nausea and headache on the first day of treatment, which subsided with sedative treatment (chloretone) on the third day. The sedative was then discontinued without further recurrence of symptoms. The same patient also developed generalised pruritis with erythema during the last two days of treatment. This subsided after penicillin therapy was terminated.

(3) *Skin Symptoms*—These are sometimes to be seen. One case we saw not in this series, had an angioneurotic oedema of one side of the face and chin and general urticaria following three intramuscular injections of 20,000 units each. This disappeared promptly on stopping the drug. An urticarial rash may be present and may be wide spread. On some occasions it may be very irritating, and a case under treatment, not in this series, developed swelling of the palms and soles and intense itching of the figures.

with joint pains, malaise and abdominal cramp Symptoms were relieved by the injection of $\frac{1}{2}$ cc of adrenalin chloride Some observers report erythema multiforme, herpes simplex and even exfoliative dermatitis Generalised pruritus and "id" eruptions on the palms and soles have also been reported Other milder forms of skin eruption do occur, but are usually not severe enough to warrant interruption of treatment

Follow Up—This has proved an extremely difficult problem, and the patient who has been relieved of his symptoms in a short period of stay in a hospital, during which time he has been subjected to a series of three-hourly pricks, blood examinations and lumbar punctures, is reluctant to come up for further investigations and its attendant discomforts, when he feels quite well Some of our cases have refused lumbar puncture even during the period of their admission Some of these patients in the absence of a "follow up" may later develop into a state of sero-positive latency in which there is no clinical evidence of the disease but a persistently positive blood serology In this state the patient may think himself cured but is capable of transmitting his disease to others In the army, the "follow up" after penicillin treatment requires blood tests at the 2nd, 4th, 6th, 9th, 12th, 18th and 24th months, and C.S.F. examinations at the 6th and 18th months

Some Problems—A most important problem is that of masking early primary syphilis during its period of incubation, if penicillin is prescribed for an associated Gonorrhoeal infection This will mean "follow up" of all gonorrhoea patients for signs of syphilis, for some months after they have recovered from their original infection Perhaps it would be better if as a routine in all cases of early gonorrhoea with a history of recent exposure, that treatment with one of the "sulpha" group of drugs should be given a trial first During this period of trial and subsequent "follow up" several cases of primary syphilis might be disclosed which might have remained masked had penicillin been tried in the first instance In the army the "follow up" after penicillin treatment for gonorrhoea requires blood tests at 1, 2, 3 and 4 months and a blood and C.S.F. at 6 months

A second consideration is that of cost We have been limited in our choice of cases by the ability of the patient to pay for his own penicillin which has been quite a problem for most of them It is possible that in the near future, prices will drop and the drug become available to a greater number of people This in turn will give rise to another problem, viz, that of accommodation Naturally, with injections given every three hours patients have to be warded for at least eight days It is impossible to treat them as ambulatory cases under present conditions Penicillin in oil has not proved very consistent and is not at present an answer to the problem It is also prohibitive in price and unsuited to hospital out-door usage on account of the elaborate technique involved in giving it It is also present experience that the series of peaks given by the three-hourly intramuscular method, gives better results than by continuous therapy which gives a more constant blood level

Another problem at present is that of the instability of penicillin and the difficulty of storage. The present ice-box system in the wards, is not ideal, especially when the drug has to be kept for several days as is the case with bulbs containing 500,000 units. Ice-boxes are continually being opened and other articles are being constantly added to them and this must expose the penicillin to variations in temperature which would naturally detract from its potency. A very important point is the method of its transport from abroad to this country. Is this done under ideal conditions? Recently I had been with a colleague to purchase some penicillin which had been flown over from America. It was disclosed that this penicillin had not been refrigerated during its journey here and it is conceivable that its potency must have diminished as a result.

We have never in choosing our cases, lost sight of the fact that the standard long-term treatment of early syphilis is a well tried and proven method of treating the disease. Our cases have been chosen from amongst those who were intolerant to the older remedies or showed no improvement under them or, as in our cases of congenital syphilis, penicillin was considered to have a greater margin of safety, or these people unable, from the nature of their employment, to take regular treatment.

In conclusion we would like to quote a dictum of Stokes "From A.D. 1943 it will take a year to guess, two years to intimate, five years to indicate and a decade or more to know what penicillin does in syphilis."

DISCUSSION

Dr. J. C. Patel asked whether there was any probability of the *Treponema pallidum* becoming penicillin resistant on a lower initial dosage. He added that in the purer forms of penicillin there was no need of refrigeration for storage.

Dr. J. A. Fernandez replying said that it was too early to say whether resistance to penicillin developed in certain cases. He added that experimentally in animals resistance to penicillin could be produced.

Dr. A. C. Rebello congratulated the speakers on the work done and then mentioned his experiences at the Wadia Children Hospital where he obtained good clinical results with penicillin in congenital syphilis.

A CASE OF TUBERCULOSIS OF CONJUNCTIVA

C. B. DHURANDHAR

K. E. M. Hospital BOMBAY

Because of the rarity of the lesion, it is thought desirable to publish the following case.

Miss G. R. a female, Hindu, aged 10 years was admitted in the wards for foreign body sensation in both eyes, sticking up of lids and a painful swelling of the cheek in front of left tragus.

On examination the tarsal conjunctiva of the upper lids showed coarse round nodules, red in colour and rather soft in consistency. The follicles in both the lower fornices were bigger and more prominent than those on the tarsal conjunctiva and were irregularly distributed. There was some mucopurulent discharge. Vision in both eyes was 6/8 dots.

The rest of the structures of eye and its adenexa were normal.

Left preauricular gland was enlarged 1 inch x 1 inch, hot, tender, painful and soft in consistency. It was freely moveable.

over the underlying structures but the skin over it was slightly adherent. The left sub-maxillary, axillary and the glands in the groin were enlarged.

The patient appears to be well built and well nourished. The present complaint started with painful swelling left cheek 3 months back. One month after the swelling both the eyes—first left and then right—became red and painful. Subsequently the pain disappeared and for last one month patient is having foreign body sensation in the eyes and sticking up of lids. There is no history of fever or cough or any previous acute illness.

X-ray examination of chest does not show any abnormality.

Laboratory Investigations

(1) Smear of Conjunctival discharge stained by Gram's & Ziehl Neelson method—Negative (2) Smear of biopsy material stained by Ziehl Neelson method—Negative (3) Cultural examination done—Results awaited

(1) Biopsy report—Changes of tubercular inflammation. No tubercle bacilli could be detected. (2) Sedimentation rate—57 mm per hour (Normal 0–6 mm). (3) Cytological examination of blood—Total count—R.B.C 3,800,000 c mm, W.B.C 9,500 c mm, Haemoglobin 86.4 per cent, Colour Index 1.1. (3) Differential Count—Polymorph nuclear 66%, Eosinophils 65%, Eosinophils 1%, Mononuclear 34%, Large mononuclear 2%, Lymphocytes 32%.

Diagnosis—Nodular type of tubercular inflammation of Conjunctiva. *Differential Diagnosis*—The condition has to be differentiated from spring catarrh, trachoma, periauricular, oculo glandular syndrome, Benign lympho-granuloma and conjunctival tuberculides. The hard feel of follicles, milky white appearance of conjunctiva and itching sensation which are characteristics of spring catarrh are absent in this case. Absence of pannus rules out the diagnosis of trachoma. In periauricular's syndrome the lesion is usually of an acute type, unilateral and the lids are markedly swollen, hard, painful and tender. In benign lymphogranuloma there is no caseation. The conjunctival tuberculides alone as such do not show tissue necrosis (Benign millary lupoid). In the absence of tubercle bacilli in various smears and in biopsy section, the diagnosis can be confirmed only by results of animal inoculation and cultural examination.

Treatment—The various types of treatments suggested are excision of growth followed by cauterisation, ultraviolet rays exposures and injection of tuberculin. We propose to treat this case on tuberculin.

Progress—Usually prognosis in such cases is not good. The lesion progresses to the other structures of the eye and then disseminates to other parts of the body.

The tuberculosis of conjunctiva is not so common and particularly the nodular variety is rather rare. In the absence of tubercle bacilli whether this condition could be diagnosed as tuberculosis of conjunctiva or whether it is allergic, secondary to glandular infection is rather problematic.

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Original Contributions

IMMEDIATE TOXIC REACTIONS OF MERCURIAL DIURETICS AND THEIR PREVENTION

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Two sudden deaths were reported from the V J Hospital, Amritsar by Dr Baloch after the use of Neptal. The following are brief histories of the cases

Case No. 1—A middle aged man suffering from congestive heart failure admitted into the Medical Ward was given 1 c.c. of Neptal intramuscularly followed by 2 c.c. of Neptal intramuscularly on the 6th day. Both injections were followed by diuresis without any untoward effect. The third injection was given about the 12th day when 2 c.c. of Neptal diluted in 10 c.c. of 25% glucose were given intravenously slowly. The patient showed dyspnoea, cyanosis, imperceptible pulse and expired within 2 minutes.

Case No. 2—A middle aged woman suffering from congestive heart failure was admitted into the Female Medical Ward. She was given 1 c.c. of Neptal intramuscularly which produced diuresis. On the 6th day she was given 2 c.c. of Neptal diluted with 10 c.c. of 25% glucose slowly intravenously. She expired within 4 minutes of the injection.

BRIEF REVIEW OF THE RELEVANT PAST WORK

We read all the relevant literature in the various books and journals available to us.

The following features of this type of reaction have been described by Pines, Sanabria and Arriens

- 1 They manifest themselves in the clinic only after the intravenous route of administration

- 2 They appear very soon after the injection is over, generally from a few seconds to five or at the most ten minutes and stop within a very short time if they are not fatal

- 3 There is experimental and clinical evidence to show that these reactions occur because of disturbances in the specific heart musculature and perhaps also in the active musculature of the ventricles

- 4 The peripheral vascular collapse was not observed during these reactions, and therefore they are probably not of an anaphylactic nature (Wexler and Ellis)

Twenty-six cases were analysed by Degraff and Nedler (1942), beginning from Redlich's cases reported in 1926. To these may be added two cases of Levin, and now these two cases of Dr Baloch.

In the two cases communicated by Dr Baloch the injections were given slowly and it is therefore unlikely that the deaths resulted from a technical error.

In 1911, Mueller, Schoeller and Schrauth described immediate death in cats with mercurial compounds. In 1922, Salant and Kletman showed that inorganic and organic mercury salts produce disturbances of heart action in a turtle's perfused heart. They showed too that in dogs "dilatation cordis" resulted from the intravenous injections of inorganic mercurial salts and mercurochrome. In 1926, Jackson reported that 5 cc of a 2% solution of salyrgan, given intravenously, produced regularly, within 3 to 5 minutes, the death of normal dogs through ventricular fibrillation.

Chastain and Mackie in 1940 administering large intravenous doses of Esidrone to normal dogs under barbiturate anaesthesia, observed within 12 to 15 seconds after the injection, deviation of the T waves, followed by ventricular flutter, fibrillation and death.

In 1942, Barker, Lindberg and Thomas gave various mercurial diuretics intravenously to thirty normal dogs, with and without intravenous barbital anaesthesia. Death was produced by ventricular fibrillation.

Wexler and Ellis state that there is strong clinical evidence to show that in man the mechanism of fulminant reaction to the intravenous injection of mercurial diuretics is exactly the same as in the case of animals and that at present, there is no known way of preventing fatal reactions.

The following statement is annotated in the *British Medical Journal*, October 31, 1942 —

"On some occasions there is clinical evidence of a disordered action of the heart, with forceful, irregular ventricular beats. This is comparable to the effect of injecting an excessive dose of the mercurial diuretics in healthy dogs or cats in which electrocardiograms and direct observation show depression of the T wave and extrasystoles, followed by ventricular fibrillation and death."

Recently, in 1944, Ignacy Pines, Antonio Sanabria, and R. T. Hernandez Arriens have carried out experiments on dogs with the idea of finding out whether certain substances, if added to the mercurial diuretics, could prevent fatal reactions in human beings. They came to the conclusion that —

1 Quinine Sulphate has not only no hindering effect upon the development of ventricular fibrillation after mercurial diuretics but on the contrary it rather accelerates it.

2 Magnesium sulphate has a suppressing effect upon the ventricular fibrillation provoked by the administration of mercurial diuretics.

They observed a very favourable action of 0.5 cc of a 20% solution of magnesium sulphate upon the course of heart intoxication due to intracardiac or intravenous injection of Esidrone.

We have experimented on thirty dogs, repeating some of the experiments already done and trying some new experiments to find out some method which could lessen the risk of such reactions. We have not completed our investigations yet and there is a large number of drugs which we mean to try as soon as they are available.

Method—All the experiments were carried on dogs under Paraldehyde anaesthesia, 2 cc per Kg and 25 cc per Kg in experiments Nos 25 and 26. In experiment No 24 the anaesthesia was supplemented by whiffs of Ether. In some of the experiments the chest was opened and artificial respiration carried on while in others simple blood pressure tracings were considered to be sufficient and so the chest was not opened and no artificial respiration carried on. In a few cases the pericardial sac was opened to facilitate direct observation. The drug in every case was injected directly into the femoral vein.

We have selected 4 of these tracings to show the main results (See plate, opp p 280, figs I, II, III and IV)

The results of the experiments are given in the following table

TABLE

No	Weight of Dog	Details of Experiment	Drugs Administered	Effects	Results
1	7.3 kilos.	Normal Blood Pressure recorded. Chest opened & Artificial respiration continued. The movements of heart noted at the same time.	Neptal 4 cc I V (About $\frac{1}{2}$ cc per kilo)	Immediate slight rise in B.P. followed by abrupt fall in 20 sec. Heart became irregular followed by Vent. Fib. Dog died after 3 minutes.	Dog died in 3 minutes.
2	5.0 kilos.	do	Neptal 1.25 cc I V ($\frac{1}{4}$ cc per kilo)	Immediate rise of B.P. followed by a fall. Heart became irregular. There were systoles and a very transient Vent. Fib. The effect began to pass away and the heart became normal after 5 mins.	Dog survived after transient irregularity.
3	7.0 kilos.	do	Neptal 2.3 cc (1/3 cc per kilo)	Immediate rise of B.P. followed after 15 sec by an abrupt fall. Heart became irregular after 30 sec followed by Vent. Fib. & heart stopped after 4 mins.	Dog died after four mins.
4	9.1 kilos.	do	Neptal 1.8 cc I V (3 m per kilo)	Immediate rise of B.P. followed by a fall. The amplitude of tracings began to decrease. After 4 min it began to increase and heart was normal after 10 min.	Dog survived.
5	6.4 kilos.	Normal B.P. recorded. Chest not opened.	Neptal 1.7 cc I V (4 m per kilo)	Immediate rise of B.P. followed after 1½ min by fall. This was followed by irregularity and dog died in 2½ min.	Dog died.
6	6.9 kilos.	Normal B.P. recorded. Chest not opened.	Neptal 1.3 cc I V (3 m per kilo)	Immediate rise followed by a small fall but no irregularity.	Dog survived.
7	6.0 kilos.	do	Neptal 1.5 cc I V (3½ m per kilo)	Abrupt fall of B.P. after 2 min followed by irregularity and heart ceased beating after 3 min.	Dog died.

No	Weight of Dog	Details of Experiment	Drugs Administered	Effect	Results
8	5.4 kilos.	Normal B.P. recorded. Art. resp. contd. Movements of heart noted (chest opened)	Neptal 1.8 c.c. (1/3 c.c. per kilo) diluted with normal saline upto 10 c.c. given in 5 min	Immediate rise in B.P. followed after 5 min by irregularity of heart and after 16 min irregularity disappeared and heart became normal	Dog survived
9	3.7 kilos	do	Neptal 1.2 c.c. I.V. (1/3 c.c. per kilo) diluted with normal saline upto 10 c.c. given slowly in 5 min	Immediate rise in B.P. followed after 5 min by irregularity there was a temporary standstill followed by revival, but the heart again stopped after 18 min. Pericardium not opened	Dog died after 15 minutes
10	4.6 kilos	do	Neptal 1.5 c.c. I.V. (1/3 c.c. per kilo) diluted with distilled water upto 10 c.c. given in 5 min	Immediate rise in B.P. followed after 5 min. by irregularity of heart, followed by death in 7 min.	Dog died after 7 min
11	8.2 kilos.	do	Neptal 2.7 c.c. I.V. (1/3 c.c. per kilo) diluted with distilled water upto 10 c.c. given slowly in 10 min	Rise in B.P. followed by successive falls and rises till after 12 min. the heart stopped beating	Dog died after 12 min
12	4.6 kilos.	do	Neptal 1.5 c.c. I.V. (1/3 c.c. per kilo) given without dilution in 15 min	Immediate rise in B.P. followed after 5 min by irregularity of heart which then stopped beating	Dog died after 7 min
13	0.4 kilos	Normal B.P. recorded. Art. Resp. contd. Movement of heart noted (chest opened)	Neptal 2.2 c.c. I.V. (1/3 c.c. per kilo) with Mag Sulph 20%	Immediate but slight rise of B.P. followed by an abrupt fall. Beats became irregular after 1 min and stopped after 4 min	Dog died after 4 min
14	11 kilos	Do	Neptal 3.6 c.c. I.V. (1/3 c.c. per kilo) with Mag Sulph 1 c.c. 20%	Heart became irregular after 30 sec and ceased beating after 3½ min	Dog died after 3½ min
15	2.8 kilos	do	Mag Sulph 1 c.c. 20% I.V. After 5 min 8 c.c. of Neptal I.V. (1/3 c.c. per kilo)	Heart became irregular after 30 sec and ceased beating after 4 min	Dog died after 4 min.
16	7.3 kilos	Normal B.P. recorded without opening chest.	Mag Sulph 20% 1 c.c. immediate followed by Neptal 25½ m (3½ m per kilo)	Slight rise in B.P. followed by an abrupt fall after two min & dog died after 3 min	Dog died
17	9.1 kilos	Normal B.P. recorded. Chest not opened.	Mag Sulph 20% 1 c.c. followed by Etdrone 2.2 c.c. I.V. (Slowly)	Fall in B.P. which became normal, but the heart became irregular after 2 min and continued in that condition for a further 3½ min. Dog died after 5½ min	Dog died
18	3.7 kilos	Normal B.P. recorded. Art. Resp. contd. Movement of heart noted (chest opened)	(a) Quinidine Sulphate ½% (25 mg in all) given (b) After 15 min. Neptal 2 c.c. (½ c.c. per kilo)	Pulse Pressure increased slight rise of B.P. followed after 10 sec by fall. Heart became irregular after 40 sec and stopped after 15 min.	Dog died after 15 min.

No	Weight of Dog	Details of Experiment	Drugs Administered	Effects	Results.
19	11.9 kilos	do	(a) Quinidine Sulph 1½% (7 mg per kilo 85 mg in all) (b) After 3 min Nep- tal 4 c.c. I V (1/3 c.c. per kilo)	Heart became irregular after 40 sec. of Neptal & ceased after 3 min	Dog died after 3 min
20	18.7 kilos	Normal B P record ed. Art. Resp contd. Movements of heart noted (chest opened)	Neptal 3.5 c.c. I V (1/3 c.c. per kilo) followed by Adrena- lin Hydrochlor 5 c.c. 1 in 1,000	Heart got accel- erated after 1 min. & became irregular after 1½ min. The B P became in- effective after 5 min	Dog died after 5 min
21	4.6 kilos.	do	(a) Pituitrin 1 c.c. I V (b) After 1 min Nep- tal 1.5 c.c. (1/3 c.c. per kilo)	Heart became irregular after 1½ min and ceased beating after 5 min	Dog died after 5 min
22	9.6 kilos	Normal B P record ed. chest not opened.	Novocain ½% 1 c.c. was given I V fol- lowed after 1 min by Neptal 33½ m (3½ m. per kilo)	Heart became irregular after 4½ min and contd thus for a further 6 min after which heart became regular & dog sur- vived	Dog survived
23	6.4 kilos	do	Novocain ½% c.c. I V followed after 1 min by 23 m of Neptal (3½ m per kilo)	Heart became irregular after 3 min & conti- nued for 1 min. more. Dog died after 5 min	Dog died
24	7.3 kilos	do	Novocain ½% 1 c.c. mixed with 26 m of Neptal given I V (3½ m per kilo) in 2 min	Slight fall in B P but no irregularity and dog survived	Dog survived
25	8.4 kilos	do	Novocain ½% 1 c.c. mixed with Neptal 23 m (3½ m per kilo) Given I V in 2 min	Slight rise in B P without any irregu- larity and dog sur- vived	Dog survived
26	9.1 kilos	Normal B P record ed without open- ing chest.	Neptal 31.8 m. (3½ m per kilo) mixed with 1 c.c. of distilled water given I V in 2 min	Slight rise in B P fol- lowed by a slight fall and irregularity dog died after 3 min	Dog died

DISCUSSION

Only direct observations and in some cases only blood pressure tracings were relied on for the results

The first three experiments (Nos 1, 2 and 3) were done to find out roughly the smallest dose which could provoke ventricular fibrillation followed by a complete standstill of the heart. We arrived at the conclusion that 1/3 c.c. of Neptal per kilo of body-weight caused ventricular fibrillation followed by standstill, in a dog.

Experiments Nos 5, 6 and 7 were performed without artificial respiration and without opening the chest and they proved that even smaller doses (3½ ms of Neptal per kilo of body-weight) of Neptal could produce fibrillation. It appears that sensitivity of the heart muscle to the toxic action of Neptal increases if artificial respiration is not carried on, probably due to anoxia of the heart muscle.

Experiments Nos 8, 9, 10, 11 and 12 were done to ascertain whether dilution with distilled water or normal saline combined with

slow injection of the drug could prevent the toxic effect of Neptal on the heart. These experiments led us to conclude that dilution with normal saline and slow injection do lessen the toxicity to the heart, but the method was not altogether safe. Only one dog survived and even here irregularities were present.

After this we repeated the experiments of Pines, Sanabria, and Arriens where they used Magnesium Sulphate to prevent fibrillation caused by Esidrone. We are afraid we cannot corroborate their results. We did not find Magnesium Sulphate effective in preventing fibrillation after Neptal or Esidrone, as was stated by them. (Vide experiments nos 13, 14, 15, 16 and 17)

Next we tried Quinidine Sulphate (exps 18 and 19). In one case death was delayed, but we formed the opinion that Quinidine Sulphate could not prevent fibrillation caused by Neptal poisoning.

Our conclusion from experiments nos 20 and 21 was that Adrenalin could improve the heart poisoned by Neptal.

We now thought of trying some of the synthetic "substitutes for Quinidine" mentioned by Dawes (1946). His studies show that the "Quinidine substitutes" comprise many of the local anaesthetics and spasmolytics in common use. Some of these are very much more active than Quinidine on the isolated auricles of the rabbit.

These findings suggest that the transmission of excitation is essentially similar in auricle and sensory nerve, in that it is susceptible to a reversible depression by the same drug.

The various drugs studied are procaine, cocaine, phenacaine, butethanol, trasentin, pethidine, etc.

We used procaine for preventing the toxic effects of Neptal on the heart. (See experiments nos 22, 23, 24 and 25). We are convinced from these experiments that procaine prevents fibrillation caused by minimum lethal doses ($3\frac{1}{2}$ ms per kilo of body-weight) of Neptal when the injection is given slowly (2 minutes). Procaine does not prevent fibrillation, however, if the dose of Neptal is large (4 ms per kilo of body-weight).

Experiment no 26 showed that the dog cannot be saved by only dilution and slow injection, and procaine (exp 22, 24, and 25) was definitely responsible for preventing the fibrillation caused by Neptal.

CONCLUSIONS

- 1 Dilution and slow intravenous injection lessen the toxicity of mercurial diuretics on the heart, but cannot prevent a fatal reaction.

- 2 Adrenalin can improve the heart poisoned by Neptal.

- 3 Procaine prevents the fibrillation caused by Neptal provided the latter is given in minimum lethal doses. In view of this, it is worthwhile investigating the effect of other "Quinidine substitutes," like butethanol, pethidine, etc.

- 4 Magnesium Sulphate and Quinidine Sulphate are not effective in preventing the fibrillation caused by Neptal though the latter delays the appearance of fibrillation.

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PLATE I

FT & MALHOTRA—MERCURIAL DIURETICS

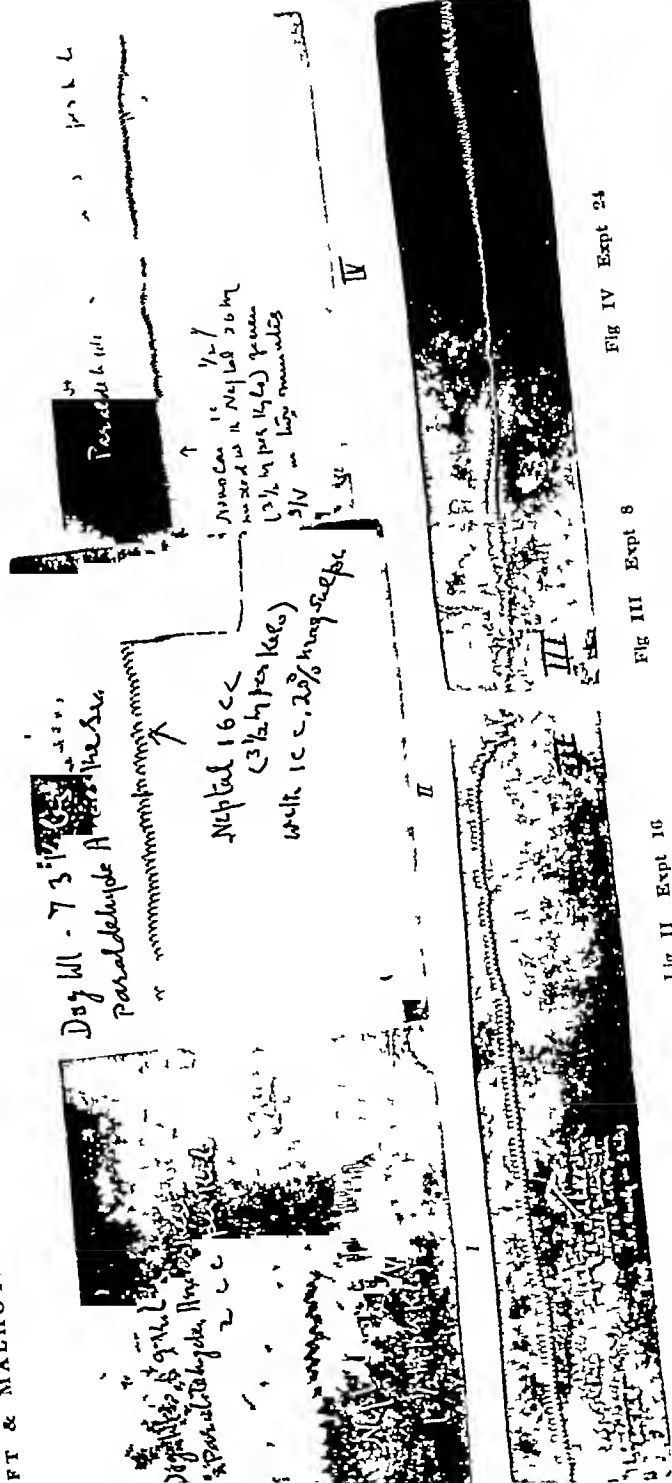


Fig III Expt 8

Fig IV Expt 24

Fig II Expt 10

HUFE-NFCROSIS OF THE LIVER

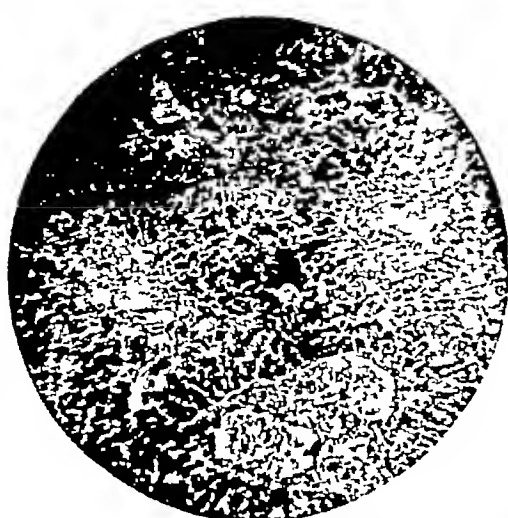


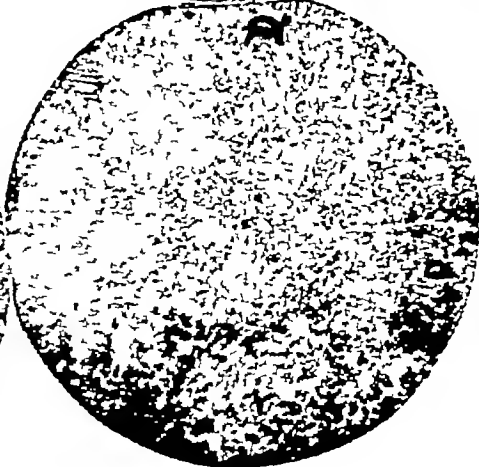
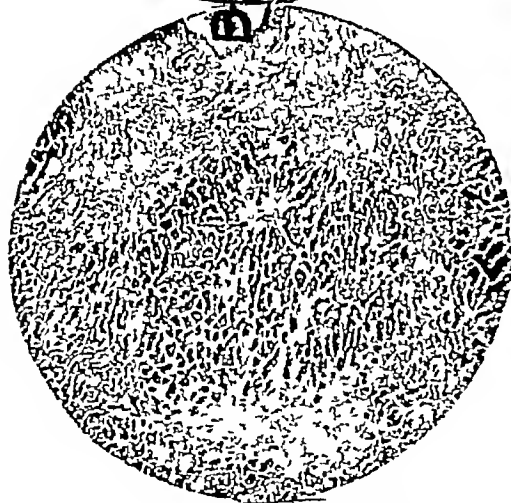
Fig A Central and midzonal necrosis in the liver lobule. The lesion resembles that of acute diffuse necrosis of the liver due to epidemic hepatitis $\times 100$ P.M. 238/43

Fig B Liver lobule well delineated by portal radiating bile ducts all round. Small foci of necrosis can be seen amidst the liver cells. The lesion resembles that of acute diffuse necrosis due to epidemic hepatitis $\times 140$ P.M. 90/142

Fig C Irregular necrosis of the liver lobules. The lesion resembles that of acute diffuse necrosis of rats produced by dietary deficiency $\times 100$ P.M. 280/43

Fig D Extensive irregular necrosis with complete wreck of the liver architecture. In the lower part of the section aggregates of mononuclears form prominent dense foci. The lesions resemble that of acute diffuse necrosis of rats produced by dietary deficiency $\times 100$ P.M. 120/46

Fig E Irregular necrosis of the liver lobules with well marked fatty changes in the liver cells. The lesion resembles that of acute diffuse necrosis of rats produced by dietary deficiency $\times 100$ P.M. 117/42



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ACUTE DIFFUSE NECROSIS OF THE LIVER*

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Acute Diffuse Necrosis of the Liver, 'Acute Necrosis', or 'Acute Yellow Atrophy' (its time-honoured name) is an anatomic and not a clinical entity, a truth which is better appreciated now than ever before, since Rokitansky²⁷ (1842) gave its first classical description. In typical cases, the lesion in the liver is unique in pathology, nothing similar occurring in any other organ. The accompanying clinical manifestations are equally striking—a severe jaundice, or, icterus gravis, and, a rapid diminution in the size of the liver.

At the moment, two questions demand urgent answers: (1) What is the pathogenesis of acute diffuse necrosis of the liver in the human being? and (2) What is its relationship with cirrhosis of the liver?

The Present Concept of the Pathogenesis—Any discussion of the pathogenesis of the disease process, by logic, involves consideration of the two main forces engaged in the combat: (1) the structure of the organ and its reaction to injury, and (2) the injurious agent and the nature of its action.

Arranged according to the order of increased susceptibility to injurious action, the different structural elements in the liver are the connective tissue framework (including the reticulum and the blood vessels), the biliary epithelium, and the liver cell epithelium. The capacity to regenerate is in the inverse order. Moderate damage produces mere degenerative changes in the liver cell, severe damage necrosis or its death, more severe damage involves the biliary epithelium, and, the stromal framework of the liver lobule as well. For the proper discharge of function mere regeneration is not enough, the different elements must be welded together into the normal structural unit of the organ—the liver lobule.

A very diverse group of agents seems capable of causing acute diffuse necrosis of the liver. On *a priori* grounds, therefore, it would be imperative to search meticulously for some common feature underlying all of them. Aetiologically considered, acute diffuse necrosis of the liver may be classified as follows—(i) Produced by exogenous agents, chemical and organismal, (ii) Acute diffuse necrosis occurring during pregnancy, and (iii) Acute diffuse necrosis as a deficiency disease. It is necessary to discuss these in detail.

I. Acute Diffuse Necrosis of the Liver produced by Exogenous Agents—(a) *The Chemical Poisons*—In man the commonly incriminated chemicals are alcohol, chloroform, carbon tetra-chloride, trinitrotoluene, tetra-chlorethene, arsenic, phosphorus, gold, cinchophan, etc. For convenience, the mushroom poisons and the snake venoms may also be included in this group. All of them have been shown to produce the lesion in the experimental animals. But, both in man and the animals, their action is capricious. In man, only a small percentage of those affected develops the full-blown lesion, the majority succumb to the general toxic effects of the chemical,

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and, the liver shows merely extensive fatty degeneration, or, at the most, zonal necrosis. This, latter lesion, is even more constant in experimental animals—a zonal necrosis affecting uniformly the whole liver substance.

(b) *The Organismal Agents*—Acute diffuse necrosis does sometimes occur in association with infectious diseases, e.g., pneumonia, diphtheria, typhoid fever, etc. Opie's²³ (1910) experiments showed that the activity of a hepatic poison (chemical) is intensified by a simultaneous bacterial infection. But, as far as a constant specific effect on the liver is concerned, only two groups of organisms need be considered.

The Spirochaetal Group—Pick²⁵ and Herxheimer¹⁵ believe that acute diffuse necrosis does rarely complicate spirochaetosis ictero-haemorrhagica, or, Weil's disease. But, Dawson Hume and Bedson (1917) did not encounter a single case in their large experience in the World War I. To this day the matter has remained unsettled. It is necessary to add, that, according to some, even the spirochaeta pallida, by itself, can cause acute diffuse necrosis.

The Virus Group—It may now be acclaimed as proved that the so-called catarrhal jaundice is an infectious disease—a hepatitis, or epidemic hepatitis—as it is called, caused by a virus. Jaundice following the yellow-fever vaccine administration, following the use of convalescent human serum for the prophylaxis of mumps or measles, following a compatible blood transfusion and the so-called arsphenamine jaundice are, again, as the epidemiological surveys and the transmission experiments have shown viral infections, Roholm and Iverson²⁶ (1939) by liver biopsies in living patients have proved that the lesion in epidemic hepatitis is a zonal necrosis—what Eppinger⁸ (1937) has called "an acute yellow atrophy in miniature." Dible, McMichael and Sherlock⁷ (1943) in their larger series of aspiration biopsies, further observed, that, the lesions in the other varieties of viral jaundice were indistinguishable from those of epidemic hepatitis. Fatal cases of epidemic hepatitis have been studied by many workers, among them Fox, et al¹⁰ (1942), Cameron (1943) and Lucké (1944), etc., and, all of them are agreed that the liver in such cases shows the changes of acute diffuse necrosis. This difference between the lesions in the two types of cases in epidemic hepatitis—cases which survive and cases which are fatal has not received the attention it deserves.

II Acute Diffuse Necrosis of the Liver occurring during Pregnancy—Acute diffuse necrosis of the liver is not an uncommon complication of pregnancy. It is vaguely explained as a manifestation of toxæmia of pregnancy. But in hyperemesis gravidarum and eclampsia, the liver lesions consist of centrilobular necrosis, (Ewing,⁹ 1905) and perilobular necrosis, (Mussay and Randall,²² 1933) respectively. Epidemic hepatitis affecting the pregnant female runs a much more severe course than otherwise, quite often proving fatal (Cockayne,⁴ 1912, Ballot,¹ 1859, Bardinat,² 1863, Hardie,¹³ 1889-90 and Hayard,¹⁴ 1889-90). This itself needs an explanation, as also the other fact, as to why the endogenous toxin, or the meta-

bolite (if it exists) of the toxaemia of pregnancy should, on occasions, deviate from its usual course and produce a massive necrosis

III Acute Diffuse Necrosis of the Liver as a Deficiency Disease
For an answer—a plausible answer—to some of the questions raised above we must turn from man to the experimental animal Gyorgy¹² (1944) gives priority to Curtis and Newburg⁵ for producing hepatic necrosis in rats by dietetic means—large doses of cystine Welchselbaum³⁰ (1935) was the first to produce hepatic lesions by dietary deficiency alone, he fed rats on a low casein diet Gyorgy and Goldblatt¹¹ (1939), by feeding young rats on diets devoid of vitamin B, but supplemented with thiamine riboflavin and pyridoxine could produce changes in the liver “resembling acute and subacute yellow atrophy”, and, changes “resembling acute and precirrhotic changes due to carbon tetrachloride” Gyorgy¹² (1944) later explained, that, the effect was due to low food intake by the animals, associated with a low casein intake Himsworth and Glynn¹⁶ (1944) then claimed, “It is possible not only to construct diets which will cause necrosis in 100 per cent of animals (rats) but also, by varying the protein content of the diets, to vary the speed of development and the severity of the lesion” They found that casein was protective, and, ultimately tracked down this property to the amino-acid, methionine, in casein Experimental dietetic necrosis, is then a deficiency disease

The Role of Dietary Deficiency in the Causation of Acute Diffuse Necrosis in Man—The results of the experimental work are so spectacular as to move the hardest sceptic to think of their implications in man Is it possible that the capricious behaviour of the exogenous chemicals in causing acute diffuse necrosis be determined by dietetic factors? Opie and Alford²⁴ (1914) have demonstrated that carbohydrate diets reduce, while, fat diets increase the susceptibility of dog's liver to chloroform The carbohydrates act by sparing the proteins Whipple²⁹ (1940) and Miller and Whipple²¹ (1942) have shown that protein depletion enhances this susceptibility, while, repletion with protein and especially certain amino acids reduces it For the acute diffuse necrosis caused by the viruses the evidence is even more convincing Epidemic hepatitis behaves quite unlike epidemics of virus origin the incubation period is long—(20 to 40 days or more) the outbreak is never explosive, the mortality is low (0.2 to 0.5 per cent), and, the fatal cases do not crop up at the height of the epidemic, indicating that the virulence of the virus is not raised by the serial animal passage McCallum & Miles²⁰ (1945) experiments are most significant Material from cases of epidemic hepatitis was injected into rats fed on diets deficient in proteins Animal passage of the virus was maintained in this manner The interesting observation was the development, late in the series, of fatal acute necrosis in the liver of animals kept on deficient diets, while, their well-fed brothers came out unscathed A foetus, living in its mother's womb as a merciless parasite, can condition a deficiency in a pregnant female subsisting on a minimal protein intake, or, enhance a deficiency already existing The deleterious effect of pregnancy in epidemic hepatitis is not difficult to appreciate, by the

same token, the zonal necrosis of toxæmia of pregnancy seems to have good opportunities to blossom into a massive type

In an attempt to apply the results of animal experiments to man Himsworth and Glynn¹⁶ (1944) have put forth a new concept To the necrosis produced by the direct action of a toxin on the liver cells they apply the term 'Toxipathic Hepatitis' This is the lesion usually seen in man in chemical poisoning, in epidemic hepatitis, and, in the toxæmias of pregnancy Histologically, it is a zonal necrosis with uniform distribution through all the liver lobules, and, if the attack is survived there is complete restitution To the necrosis due to a deficiency of nutritive factor—"but not implying that the state of deficiency can only be produced by dietary means"—is applied the term 'Trophopathic Hepatitis' Trophopathic hepatitis produced by diet alone has so far been produced only in experimental animals Histologically, this is a diffuse necrosis, and, its healing always results in a scar Now it so happens that in man acute diffuse necrosis occasionally complicates illnesses caused by agents which commonly produce only toxipathic hepatitis This according to Himsworth and Glynn¹⁶ (1944) is brought about in two ways (1) by interfering with nutrition and producing conditions conducive to the development of trophopathic hepatitis (2) the enlargement and the swelling of the liver in toxipathic hepatitis by interfering with the blood-supply in the organ conditions a deficiency In man, therefore, most of the cases of trophopathic hepatitis are secondary to toxipathic hepatitis

TABLE 1

Total number of cases compared with total number of P Ms year by year

Year	No of P Ms.	No of Cases
1927	161	1
1928	244	1
1929	126	2
1930	259	6
1931	217	3
1932	230	8
1933	246	8
1934	277	8
1935	280	8
1936	414	5
1937	403	6
1938	582	4
1939	580	7
1940	803	8
1941	350	
1942	844	5
1943	441	11
1944	200	8
1945	208	3

It was with this background that the material available in our department was studied in detail An added reason was the statement of Himsworth and Glynn¹⁶ (1944) that the cases of severe jaundice showing extensive necrosis of the liver studied by Hughes¹⁷ (1927), and Hughes and Shrivastava¹⁸ (1933) in the Punjab were really cases of primary trophopathic hepatitis due to a dietary deficiency of proteins, and, the cirrhosis prevalent there a final expression of the same disease process

The Material—During a period of 19 years, among a series of 6909 autopsies performed at the King Edward Memorial Hospital,

Bombay, were encountered 75 cases of acute diffuse necrosis of the liver. These cases are analysed (1) for their general features, (2) to find out if there is anything in their clinical manifestations to suggest the presence of nutritional deficiency, (3) to find out if the lesion, or, lesions in the liver possess any specific characteristics which may assign nutritional deficiency a place in the pathogenesis of the disease process.

TABLE 2
Age Incidence

Age in Years	No. of Cases
0 to 9	5
10 to 19	7
20 to 29	22
30 to 39	23
40 to 49	11
50 to 59	5
60 to 69	2

Youngest: 9 months
Oldest: 60 years

The General Features—Table No. 1 gives the distribution of the cases studied in the period under survey. Out of 75 cases, 66 are Hindus, 7 Mohomedans, and 2 Christians. All of them appear to come from the poorer strata of society, which is natural in an institution catering essentially for the poor. Table No. 2 shows the age incidence, the 3rd and the 4th decades seem to bear the brunt

TABLE 3
Symptoms, Signs, State of Nutrition

	CLINICAL MANIFESTATIONS	No. of Cases
Symptoms	Unconsciousness	46
	Jaundice	38
	Fever	30
	Gastro-Intestinal Symptoms	
	Vomiting	5
	Diarrhoea	8
	Pain in Abdomen	4
	Bleeding per Rectum	1
	Convulsions	5
Signs	Icterus	75
	Petichae on the Skin	4
	Liver: Palpable	0
	Enlarged*	3
	Not felt	28
	Demonstrated diminished in size	4
	No mention of liver	24
	Spleen: Enlarged	22
	Not felt	41
	No mention of spleen	12
	Ascitis*	4
	STATE OF NUTRITION —	
	'Emaciation'	32
	'Poor'	6
	'Normal'	31
	No mention	0

*Cases of Multiple Nodular Hyperplasia.

of the attack but no other inference can be drawn. Out of 75 cases 60 were males and 15 females. In view of the fact that the female admissions to the hospital are much low compared to the male ones, and, also because the hospital does not possess a maternity section, the figures cannot be considered truly representative.

The Clinical Manifestations—As judged by the duration of the symptoms, for which the patients sought admission, the onset may be described as acute. By the same criteria, the duration of the whole illness was under 6 days in 33 patients, under 10 days in 14, under 14 days in 9, and over one month in 5. The last group is composed of cases which are properly classified as the so-called sub-acute necrosis of the liver. In the remaining 14 cases the duration cannot be computed from the data available.

TABLE 4
P. M. Findings

Liver Weight in Gms	No of Cases	Spleen Weight in Gms	No of Cases	Ascitis
Between 300 & 400	2*	Between 50 & 100	—	In 9 cases
" 400 & 500	3*	" 100 & 200	30	
" 500 & 600	4	" 200 & 300	8	Serious Fluid
" 600 & 700	15	" 300 & 400	8	120 to 1200
" 700 & 800	15	" 400 & 500	2	ccs in 8
" 800 & 900	5	" 500 & 600	2	cases, Puri
" 900 & 1000	8	" 600 & 700	2*	lent Fluid
" 1000 & 1100	6	" 700 & 800	2*	in 1 case
" 1100 & 1200	11	Not Recorded	14	
Not recorded	6			

* In children under 10 years

*In Multiple Nodular Hyperplasia

TABLE 5
Associated Findings

P. M. FINDINGS	No of Cases	CLINICAL FINDINGS	No of Cases
Acute Pancreatitis	1	Epithelioma Tongue	1
Ankylostome Infection	1	Arsenical Poisoning	1
Bacillary Dysentery	1	Chloroform Poisoning (?)	1
Lobar Pneumonia	1	Snake bite	1
Bronchio-pneumonia (Terminal)	2	Pregnancy Toxaemia	3
Septicaemia	1		

The P. M. Findings—The relevant anatomical findings are illustrated in Table No. 4. It is possible that some of the 'associated findings' in Table No. 5 like acute pancreatitis, ankylostomiasis, bacillary dysentery, epithelioma tongue, etc., might have conduced to produce some nutritional deficiency, but, on the whole, nothing distinctive can be made out.

The Lesions in the Liver—The focus of attention is, of course, the liver. Most of the specimens were not available for re-examination, but, from the descriptions of the macroscopic appearances recorded certain deductions may be drawn. The striking change is the marked reduction in the weight of the organ, however, (see

Table No 4) in 17 out of 69 cases, in which it has been registered, it is seen falling within the normal range, or, very near it Lucke¹⁹ (1944) had a similar experience in one-fourth of the cases in his series. Such livers come from patients who die early in the course of the disease and consequently show early histological alterations, or, from patients who die late and histologically the organs show the changes of multiple nodular hyperplasia. Apart from the weight, the appearance of the organ varied depending again on the stage of the disease process, all the features of 'acute yellow atrophy' and 'multiple nodular hyperplasia' either singly, or in combination can be easily recognized in the descriptions.

It was argued, that, barring a few cases, (see Table No 5) where the predisposing or, the exciting cause could be at least suspected, the rest belonged to the group of the so-called 'cryptogenic acute yellow atrophies'. From the data available, it was felt that these cases could be either due to epidemic hepatitis ('toxipathic hepatitis' of Himsworth and Glynn), or due to nutritional deficiency ('trophopathic hepatitis'). Could it be possible to sort out these two types on the basis of the histological characteristics of the lesions?

TABLE 6

Comparison of Liver Lesions in the Rats* on Deficient Diet and Man* in Epidemic Hepatitis

The Lesion	In Rat	In Man
1 Parenchymatous Degeneration of the Liver Cells	Present	Absent or not conspicuous
2 Fatty Changes in the Liver Cells	Present	"
3 Central and Midzonal Necrosis in the Liver Lobule	Present	Present
4 Haemorrhages in the Necrosed Areas	Present	Present
5 Inflammatory Cells in the Necrosed Areas	Present	Present
6 Distribution of the Lesions in the Liver	Not Uniform	Uniform
7 Endophlebitis of the Central Vein of the Liver Lobule	Not Described	Described
8 Liver Lobules outlined by the Proliferating Biliary Ducts	Not Seen	Typical of this type

* Gyorgy and Goldblatt (1939)
Gyorgy (1944)

* Bauduin Lucke (1944)

Gyorgy and Goldblatt¹¹ (1939) and Gyorgy¹² (1944) have described exhaustively the lesion in the liver of the rats fed on protein deficient diets. Lucke¹⁹ (1944) has published the largest series of fatal cases of epidemic hepatitis, with a detailed account of the autopsy findings. Table No 6 has been compiled from these authors and brings forth the significant features on which, perhaps, a distinction may be based. The criteria employed in our study were these (1) Is the necrosis of the liver cells uniform and regular (central and mid-zonal) with a faint outline of the architecture still preserved, or, is the necrosis extensive, irregular, with a complete wreck of the lobular pattern? (2) Is there a delineation of the affected liver lobules by proliferating biliary epithelium? (3) Is there conspicuous fatty change in the liver cells that remain intact? A necrosis that is regular and uniform, with the liver lobules well

outlined by the proliferating bile ducts, and absence of marked fatty changes are the features characteristic of epidemic hepatitis in man (Lucké), while, irregular extensive necrosis, with no attempt to outline the liver lobules by the bile ducts, and presence of marked fatty changes in the liver cells are the features of acute necrosis produced in rats by deficient diets (Gyorgy)

Out of the 75 cases presented in this paper, sections of the liver from 56 cases were available for study. This material was scrutinized carefully, and, on the basis of the criteria outlined above, an attempt was made to classify the cases into the two groups. Table No. 7 gives the results of this investigation.

TABLE 7
The Grouping of Cases

DIAGNOSIS			No. of Cases		
MULTIPLE NODULAR HYPERPLASIA			2		
UNCLASSIFIED			6		
CLASSIFIED			48		
GROUP A	Human Epidemic Hepatitis*	10	GROUP B**	Rat Dietetic Necrosis*	38
DETAILS			DETAILS		
	Emaciated	5		Emaciated	12
	Ankylostome Infection	1		Ankylostome Infection	1
				Malaria	2
				? Chloroform (after Mastoidectomy)	1
				Septic Peritonitis	1

* Lucké (1944)

* Gyorgy and Goldblatt (1939)
Gyorgy (1944)

** In 14 cases there was no marked fatty change

Discussion—It is obvious that the presence, or, the absence of emaciation has no bearing on the group to which a case might belong as determined by the histological changes in the liver. It is well known that the general nutritional level of an individual is hardly of any use in detecting the presence of any specific deficiency. In the group resembling the rat dietary necrosis is seen a case showing coincident ankylostome infection, but, in the absence of even a blood count to prove that the parasite was affecting the host by its presence, its role in predisposing to acute necrosis of dietary origin cannot be justly assessed. In two cases there was co-existing malarial infection: in one case chronic (as judged by the presence of a big spleen, and the presence of pigment alone in the viscera), in the other case acute (as shown by the presence of the parasite in the viscera). Hughes¹⁷ (1927) has described acute hepatitis with diffuse necrosis in subjects of chronic malaria in the Punjab. In the same group it is interesting to find one case due to chloroform poisoning, the experiments of Whipple and his school^{21,29} (1940, 1942) quickly appear before one's eyes.

We have no hesitation in affirming the existence of the two types of histological changes described above, in the material we have studied. Whether they are two distinct changes, or, merely the two extremes, or even phases of the same disease process, is a question we are unable to answer. Distinction based wholly on morphology may be misleading. To deduce, from the evidence available that the two types of changes described represent the two conditions, toxipathic and trophopathic hepatitis respectively, as described by Himsworth and Glynn¹⁶ (1944) would be wholly inaccurate. But, uncomplicated dietary deficiency may have been responsible for some of the cases at least is a possibility that cannot be utterly denied. In the rest, the primary process may have conditioned a deficiency and thus produced a fatal termination. In any case, in the treatment of the severe jaundice, the administration of methionine by mouth or intravenously, together with vitamin B complex, (Gyorgy¹² (1944) and the advisability of putting the patient on a high protein, a high carbohydrate, and a low fat diet, are measures well worth a trial.

That by deficient diets alone, necrosis and cirrhotic lesions of the liver, similar to those in man, can be produced experimentally, is no mean advance. How far could the results of this experimental animal work be usefully applied to man is a matter that can be decided by a combined effort of the physiologist, the biochemist, the clinician, and the pathologist.

CONCLUSIONS

1. The lesions in the liver from 56 cases of acute diffuse necrosis have been studied histologically.

2. Two types of lesion are described (a) resembling that of acute diffuse necrosis due to epidemic hepatitis, (b) resembling that of acute diffuse necrosis in rats due to dietary deficiency.

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TREATMENT OF PERITONITIS

A REPORT OF SEVEN CASES TREATED WITH PENICILLIN AND SULPHONOMIDES

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The generalised peritonitis is considered a serious condition of abdomen. The chances of recovery depend upon the early diagnosis, early surgical intervention, the organ perforated, the general condition of the patient and the care of the patient during the post-operative period. It has usually a high mortality. The chances of survival did improve with introduction of sulpha drugs. This drug may be used locally in the peritoneal cavity, it may also be given orally when possible but the best method is to administer it parenterally. The toxic effects of sulpha drugs was a grave handicap in the use of the drug in these cases. Table I shows the cases treated with sulpha drugs in the K E M Hospital since 1943 after they were given the necessary surgical treatment. Out of a total of 27 cases 8 survived. Those who survived had an average stay of 39 days in the hospital. With the introduction of penicillin in our armamentarium the chances of survival have improved as can be seen from this preliminary report of seven cases. There are very few reports of the use of penicillin in generalised peritonitis even those are conflicting.

The use of penicillin has not been generally accepted as an effective measure in the treatment of peritonitis. This belief is partly due to the brief and unfavourable reports of its use in peritonitis, e.g., Lyons, (1943) summarising cases treated in various United States Army Hospitals, states "Infections arising as complications of appendicitis have not been responsive to such a line of treatment although one patient showed improvement coincident with the treatment." It seems however, in the few cases reported, patients were treated late in the disease, at a time when nothing could have saved them.

Another such remark is from Jaffrey (1944) in his discussion of the use of penicillin in peritonitis in the British Army, he says, "Penicillin is usually not of value in penetrating wounds of the abdomen, most of the deaths in such instances are due to physiological causes." Another reason in strengthening this belief, is the bacteria found in perforative peritonitis show a preponderance of gram negative organism which are resistant to penicillin. But it must not be forgotten that it is a mixed infection and as such it contains other organisms which are susceptible to penicillin. It is also believed that penicillin injected intramuscularly, does not reach the serious cavities. This is not wholly true in the case of the peritoneum. Five patients suffering from ascitis were injected with penicillin intramuscularly and their ascitic fluid was withdrawn and when examined, showed penicillin in enough quantity.

To be effective, penicillin treatment in peritonitis must be started early. This was proved by the experimental work of Fauley et al

A paper read at the 61st meeting of the Seth G S Medical College and K E M Hospital Staff Society on Saturday July 13 1946 with Dr A. E. DeSa in the chair

(1944) These workers produced peritonitis in dogs by ligating all blood supply to the appendix. One group received penicillin within one hour following the operation, the mortality rate was 0%. The second group received penicillin after 12 hours. The mortality was 21%, the third group received no penicillin, the mortality rate was 92.6%. These experiments prove conclusively the importance of starting treatment early in the course of disease. It also proves that penicillin reaches the peritoneal cavity.

It seems that the best method for treatment of generalised peritonitis is to instill penicillin in peritoneal cavity at the end of the operation and then subsequently to inject it through a rubber catheter introduced through the drainage tube every three hours. Kalisova (1944) reports a case where a child aged 4 years and 11 months with perforation, gangrene and general peritonitis following appendicitis was treated by this method with dramatic effect.

TABLE I
Cases of perforative peritonitis treated in K.E.M. Hospital since 1943

Cause and organ perforated	Sulfa group only			Penicillin & Sulfadiazine		
	Total	Expired	Lived	Total	Dead	Living
Typhoid	5	4	1	1	1	
Duodenum	3		3	1		1
Appendicitis	6	4	2	3		3
Trauma	4	3	1	1		1
Perforation of ileum	~	6	1	1		1
Gall bladder	1	1				
Large bowel	1	1				
	27	19	8	7	1	6
Average stay in hospital in days		39			15	

In these series of seven cases all were males, the youngest was 18 years and the oldest of 61 years. Five were operated immediately after admission. One within 24 hours and one was not operated at all. The anaesthetic used was intratracheal ether in 4 cases and the same combined with local intercostal block in two cases. On operation the peritoneal cavity was drained and the perforation was sutured. The abdomen was closed with adequate drainage. The report of the fluid from peritoneal cavity was available in two cases. The following routine post-operative treatment was given. Wangen Stien's method was adopted in all cases of aspiration of stomach contents and continued till the contents of stomach was clear, glucose saline 1000 c.c.s to 2000 c.c.s was given daily to all the patients. Blood transfusion was given in one case and plasma transfusion in two cases. (Its use was dependent on its availability). The penicillin was given in all the seven cases. It was given by intramuscular injection in the dosage of 50,000 units initially and 30,000 to 50,000 units every 3 hours. The total dosage varied from 9,80,000 to 1,500,000 units. The penicillin was not used intraperitoneally on the operation table as the drug was not available till some time after the

operation and subsequently when an attempt was made to inject it through the drainage tube, it was often found to be blocked by lymph flakes

The use of penicillin in cases of generalised perforative peritonitis is debatable. The culture of the peritoneal exudate shows predominance of gram negative organism (*B. coli*, *B. portei*, *B. welchii*, *B. Pycocynae*) these organisms are penicillin-resistant and they liberate an enzyme penicillinase which destroyed the drug rapidly. The high dosage was used in the hope that even if a major part was destroyed by this enzyme some of it would be left to deal with other susceptible organism present and their toxins. Even though theoretically the penicillin is not indicated, the results in the present series suggest that it is of definite value in reducing the mortality of peritonitis.

TABLE II

Case No	Organ perforated	Duration of tempe- rature.	Sex & Age in years	Maximum Tempe- rature	Stay in days	Anaesthesia	Result
1	Appendix	8	M/18	103°	23	Intratracheal Ether	Cured
2	Duodenum	4	M/61	100	23	Intercostal block with supplement general	Cured
3	Appendix	5	M/18	101°	10	Not operated	Cured
4	Ileum (typhoid)	6	M/55	104°	6	Local and general	died
5	Ileum	4	M/40	102.5°	12	Intratracheal Ether	Cured
6	Appendix	6	M/23	101.6	10	Intratracheal Ether	Cured
7	Stab wound, colon Duodenum and open pneumothorax	8	M/25	100.5°	20	Intratracheal Ether	Cured

Sulpha drugs — Sulphadiazine and soluseptisine both were used parenterally. It was given in the dosage of 2 gms in all cases. Bigger (1944) has found that effects of penicillin is enhanced by its combination with sulpha drugs. The later drug alone is not sufficient as seen from Table I. The proof that penicillin is effective in reducing the mortality in generalised peritonitis cannot be conclusively ascertained as it was administered along with sulpha drugs. But it can be surmised that reduction in mortality was most probably due to penicillin and not due to sulpha drugs, because the sulpha drugs were given in such a small dosage and when given alone in high dosage as above mentioned the mortality was still high. Besides the reduction in mortality other advantages of penicillin therapy were evident in this series. There was marked improvement in the general condition of the patient. He was less toxic. There were no post-operative pulmonary complications even though ether was used as a general anaesthetic. Even where there was an open pneumothorax in one case in addition to stab wound in abdomen the recovery was uneventful. In none of the cases there were any reactions due to penicillin. Another advantage of the penicillin therapy is to reduce the period of stay in the hospital. The average stay in the hospital in the present series is 15 days as compared to 39 days in a series treated by sulphonamides alone.

SUMMARY

- 1 A brief review of the use of penicillin in the treatment of peritonitis is given
- 2 Seven cases of generalised peritonitis treated with penicillin and sulpha drugs are reported
- 3 The results in the present series cannot be said to be conclusive as the number is small but nevertheless encouraging

Case No 1 A male aged 18, was admitted for pain in the abdomen of eight days duration which had increased in intensity in the last two days. He was cyanosed, very toxic and there was rigidity and tenderness over the abdomen. Peristaltic sounds could not be heard. The laparotomy was performed under general anaesthesia. Large amount of pus and a faecolith of the size of $1 \times \frac{1}{2}$ cm was found in the right iliac fossa. The faecolith was removed but not the perforated appendix. The peritoneal cavity was drained. He was given a routine treatment of (1) continuous suction of stomach contents (2) glucose saline 1500 daily for 5 days. (3) Penicillin. The 40 000 units of penicillin 3 hourly with an initial dosage of 50 000 units. The total dosage of penicillin was 1 800 000 units in 5 days. 20 c.c. of 10% sulpiciceno was also given daily, for 6 days. Toxicemia lessened in 48 hours. Temperature touched normal on the 8th day. He had no surgical or pulmonary complications. His total stay in the hospital was 23 days.

Case No 2 A male aged 61 years was admitted for moderate pain in abdomen for 8 days which had increased during last 24 hours. On admission he was toxic had dry tongue with a feeble pulse of 120 per minute and with a low general condition. On examination he had rigid abdomen with tenderness in epigastric region. There were no sounds in the abdomen. The operation was performed with local inter-costal block anaesthesia along with general. On opening the abdomen a big sized perforation was discovered in the duodenum which was transversely sutured. He was given a routine treatment of (1) continuous suction of stomach contents. (2) glucose saline 500 c.c. daily for 5 days. (3) 500 c.c. of plasma daily for 3 days. (4) Blood transfusion of 500 c.c. once. (5) Penicillin 1 040 000 units in 4 days. Temperature touched normal on the 5th day and was discharged on 23rd day. There were no complications.

Case No 3 A man aged 18 was admitted with pain in right iliac fossa of 30 hours duration. He had travelled 150 miles by car with pain. On examination he had marked rigidity and tenderness all over the abdomen but most marked in the right iliac fossa. Temperature 100°F . Pulse 108. Oschner-Scherren line of treatment was followed. He was given the routine treatment of aspiration of stomach and glucose saline for 3 days. 980 000 units of penicillin was given in 3 days. In addition sulphadiazine 2 gms was given daily. The temperature was normal on the 7th day and the patient was discharged on the 10 day. While performing appendicectomy on this patient two months later, adhesions were noticed in the right iliac fossa.

Case No 4 Male, 55 years was admitted for severe pain in the abdomen of ten hours duration. He had relapse of Enteric fever. He had rigidity of abdomen and there were no sounds heard. The patient was toxic and delirious. Pulse 140 per minute. Temperature 98°F . Under local anaesthesia, he was operated. The peritoneal cavity was drained the perforation in ileum was sutured. He was given routine treatment of glucose saline. 1,500 000 units of penicillin was given in 4 days. 2 gms of sulphadiazine per day for four days were given. The patient died on the 6th day.

Case No 5 Male aged 40 years was admitted for pain all over the abdomen with absolute constipation for 18 hours. The pain started after a fall while walking. He had a right inguinal hernia which was reducible at the time of admission. On examination he had rigidity all over the abdomen with tenderness round about the umbilicus. There were no sounds in the abdomen. Pulse 100 per minute. Temperature 101°F . Abdomen was screened but there was no gas under the domes of diaphragm. On operation there was perforation in the ileum which was sutured, pus drained. The culture report of the pus was that it was sterile. He was given routine post-operative treatment of glucose saline and stomach drainage. He was given penicillin 1 000 000 units in 5 days. He was given sulphadiazine by injection of 2 gm. daily. Temperature touched normal on the 6th day. There were no complications and post-operative period was smooth.

Case No 6 A man aged 23 was admitted for pain in right iliac fossa of 3 days duration. It had become worse for previous 24 hours. On examination there was rigidity all over the abdomen. No peristalsis could be heard. There was tenderness in right iliac fossa. Temperature 102°F . Pulse 100 per minute. White blood cells 17 400 per cmm. On opening of the abdomen there was about a pint of pus which was removed. The appendix which had perforated was removed. The peritoneal cavity was drained. Gram positive cocci were seen in smear and (Escherichia coli grown in culture. He was given routine post-operative treatment of glucose saline and stomach drainage. He was infused with 300 c.c. plasma. Penicillin was given initially 50,000 units and a maintenance dose of 30 000 every three hours. A total dosage of penicillin was 1,140 000 units in 5 days. He was given 2 gm of sulphadiazine by injections for 6 days. Temperature touched normal on the 7th day, and post operative period was uneventful.

Case No 7 A male aged 25 was admitted with two stab wounds, one of them had perforated hepatic flexure of colon and 2nd part of the duodenum. Second stab wound had caused open pneumothorax. Laparotomy was done under general anaesthesia (Intra tracheal ether). The perforations were sutured. The peritoneal cavity and retroperitoneal space was drained. He was given routine post-operative treatment of aspiration of stomach and glucose saline for 7 days. Penicillin (1 080 000 units) was given in usual dosage in 5 days. Two grams of sulphadiazine was given daily for 6 days. Temperature came to normal on 8th day. The drainage was removed on the 6th day. There were no complications except a bed sore.

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A CASE OF ELEPHANTIASIS TREATED BY PRIMARY SKIN-GRAFTING

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Elephantiasis has been known to the Hindus as early as 600 B C as well to the Arab Physicians. Attempts at treatment have been complete failure except some favourable sites such as scrotum. The usual fate of a patient of elephantiasis attending a general hospital is that he got admitted in the hospital when there was room, after a long waiting, and underwent a Kondoleon's operation. He was also treated with repeated courses of antimony and non-specific protein therapy. In majority of cases he left the hospital disappointed. A case of Filarial elephantiasis treated by excision followed by primary skin grafting is presented below.

Case Report —A male Hindu fifty years of age from Madras, was first seen on the 20th March 1946. His chief complaint was that he had swelling of right foot and leg for the last ten years. The swelling started after an attack of fever with rigors and has been gradually increasing ever since. He gave history of fever with rigor frequently during the last ten years for which he did not seek treatment. He had no chyluria during the period.

On examination there was slight pitting on pressure on the upper part of the right leg. The lower half of the right leg and foot showed an advanced degree of elephantiasis with eczematous skin and ulcerations at places. As the condition had not improved all this time he was willing even for an amputation. There were no other filarial manifestations. Right inguinal lymph nodes were enlarged.

Microfilaria were not detected in the peripheral blood even during rigor, in the sternal marrow and in the urine. Blood Kahn was negative. A histological examination of the biopsy showed characteristic changes of elephantiasis with fibrosis oedema and lymphocytic infiltration, with an area of calcification at one place.

Five c c of methylene blue injected into the right foot, was not excreted in the urine for 24 hours. Two c c of Indian Ink injected in the same region was not seen in the regional lymph nodes. Both these observations suggested that there was no circulation of the lymph in the lower extremity.

A method of "excision followed by primary skin grafting" has been described for elephantiasis. This method was attempted on this patient on 8-4-46. The thickened tissue was incised only on the extensor surface and completely excised till the underlying tendons were exposed. No tourniquet was used and the tissue exuded clear fluid at first like the white of a water-melon and as I went deeper blood started oozing which though it looked furious at first could be controlled by saline mops. Thiersch's skin grafts were taken from the same thigh and implanted on the raw area. On 18

grafts had completely taken and the result of the operation looked very gratifying to the patient for he could now walk about freely, felt lighter and had gained good range of movement at the ankle. The second stage was being planned but the patient insisted on being allowed to go home for a month before any further operation. Under observation the grafts started showing early elephantoid change. Bowesman (1938) had advocated use of glycerin 10% in distilled water given intra-arterially in cases of elephantiasis. He has reported 19 cases treated by this method. The rationale of the action being due to its hygroscopic property was not easily understood but because his results showed a definite diminution in the girth after injection it was decided to try this method in this case.

The first injection in the femoral artery of 2 c c glycerin was given on 28-4-46. The treatment was interrupted as the patient left the hospital against advice, even though he had developed a pleural effusion.

He was re-admitted on 12-6-46 when he came back after a month with definite elephantoid changes in the grafts and little ulceration at one place. Pleural effusion was tapped on 15-6-46. The fluid was yellow and showed both lymphocytes and polymorphs. There was no chylothorax and no microfilaria were seen in the fluid. He has received a course of glycerin injections with hypertonic saline during the last month, and the grafts have remained without further increase in elephantoid changes. The case is presented rather early as patient is likely to leave the hospital. I would like to know the opinion of others as to the advisability of doing the second stage of the operation.

In the end I must thank Dr. Munsif who has given me the fullest facilities in doing this study. I must also thank Prof. Koppikar and the anatomy department. Dr. Bhende occupies a special place in this study for he has been extremely co-operating and has personally studied the biopsy sections, the sternal puncture and it was on his suggestion that I employed Indian Ink to study lymphatic patency. I thank him sincerely for his kind help without which I could not have gone far.

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THE INDIAN PHYSICIAN

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Original Contributions

ACTION OF CERTAIN ANTIMALARIAL DRUGS ON PLASMA PROTHROMBIN LEVEL IN NORMAL AND MALARIAL SUBJECTS

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Hypoprothrombinemic action of quinine sulphate was pointed out by Pirk and Engelberg (1945), who investigated in five subjects the effect of quinine sulphate on prothrombin level Parry (1946) has emphasised the tendency to haemorrhage as an important complication of malaria. It may lead to confusion in diagnosis and to complications after operation. He advocates prompt intravenous use of quinine in surgical cases when malaria is suspected. From his case reports quoted, it is suggested that administration of quinine immediately stops haemorrhage. Laha (1945) described massive epistaxis in a case of benign tertian malaria where bleeding could only be controlled by intramuscular injection of quinine. These views appear to be in conflict with Pirk and Engelberg's (loc cit) experimental findings.

This subject is of considerable importance in the tropics where malaria is rampant, because the haemorrhagic tendency in malaria is well known. It became all the more important during the world war when the allied armies were fighting in malarial regions and were regularly getting quinine prophylaxis. With the enemy taking over the world's most productive cinchona plantations, the allied armies depended on atabrin (Russell, 1943). According to Pirk and Engelberg (loc cit) these soldiers, sailors and marines, fighting in malaria-infested regions and receiving quinine prophylaxis will have a low plasma prothrombin. On being wounded there will be prolonged bleeding and until measures are taken to increase the plasma prothrombin level, the bleeding may continue.

Due to these conflicting views on the subject, the present experimental work was undertaken. From amongst the various anti-malarials available, the two commonly used, quinine and mepacrine, were selected for this investigation. The effect of these drugs on the plasma prothrombin level has been investigated in normal subjects as well as in subjects suffering from malaria.

Technique—Since Quick (1938) described a method for estimation of prothrombin time, several modifications have been suggested. The chief objections to his method are (i) that the solution after addition of rabbit brain extract becomes opaque and the reading of

the end point (formation of fibrin web) is difficult, and (ii) the repeated preparation of fresh thromboplastin is a cumbersome process. Further the different preparations may vary in potency.

Fullerton (1940) suggested the use of venom of Russell viper as the thromboplastin instead of rabbit brain extract. Russell's viper venom possesses no group specificity in contradiction to thromboplastin derived from brain. The disadvantage of this method is that the prothrombin time is often delayed. The activity of Russell viper venom is greatly enhanced by lecithin (Quick, 1945), while the tissue extract is not affected by lecithin. Witts and Hobson (1942) advocate the addition of lecithin to the venom solution, while Page and Russell (1941) advocate its omission. According to the latter's technique viper venom and calcium chloride are added to plasma obtained by centrifuging the decalcified venous blood. The end point is characterised by the formation of fibrin particles clearly visible in the agitated test tube.

Iyengar, Sehra and Mukerji (1942) have described a modified method for the determination of prothrombin time, wherein a solution of Russell viper venom, 1 in 20,000 in 0.025 M CaCl_2 is used. This venom solution keeps its thromboplastic potency unaltered if kept under toluene at a temperature of about 5° C. This permits the employment of a stable stock solution of thromboplastin of constant potency.

In carrying out the estimations in this paper, the above modified method of Iyengar et al (loc cit) was used. According to this technique, 4.5 cc of blood is taken into a centrifuge tube containing 0.5 cc of 0.1 M sodium oxalate solution and centrifuged. After thorough mixing 0.2 cc of this plasma is added to 0.2 cc of 1 in 20,000 Russell viper venom solution in 0.025 M CaCl_2 , and kept in water bath at 37°C. The stop watch is clicked simultaneously. The tube is shaken lightly in the water bath to within a few seconds of the expected clotting time. For the accurate timing of the end point it is essential to tilt the tube gently. The first appearance of the fibrin web is the time recorded. The tube should not be shaken too vigorously, because the initial tenuous fibrin mesh is apt to be broken and thus escape detection, and more time is required for the formation of a fresh web. The average time has been 10 to 14 seconds.

Besides permitting the use of a stock solution which is of a definite advantage when a large number of samples are to be tested, this method has certain other advantages. Addition of thromboplastin in calcium chloride solution minimises the time interval of thromboplastin—prothrombin reaction and speeds up the clotting time because the volume of the reaction mixture is reduced to 0.4 cc, thereby increasing the concentration of prothrombin in the mixture by 33 per cent as compared to Fullerton's method.

R. S. Gupta working in my department has determined prothrombin time in a large number of Indians (both normal and those suffering from various diseases). He takes the oxalate solution in the syringe before drawing the blood and uses 50 per cent and 25 per cent diluted plasma. The dilution gives better results in cases of mild hypoprothrombinemia. Shapiro (1943) and Brambel and

Loker (1943) have shown that greater sensitivity is obtained in the Quick method if the plasma is diluted 12.5 per cent

ACTION OF QUININE SULPHATE ON PROTHROMBIN TIME

Five male subjects ranging in age from 25 to 38 years were chosen. They were of normal health and took a balanced diet. The premedication prothrombin time was within normal range in each case, except in one where it was slightly increased to 16 seconds. Quinine sulphate in single doses of 5 grains (0.33 g.) daily was administered orally. In all cases there was a significant rise in prothrombin time indicating a definite hypoprothrombinemic action of quinine. The quinine sulphate was then stopped and the prothrombin time regressed promptly and reached the premedication level within a short time.

Subsequently quinine sulphate was given with 10 mg of vitamin K daily, for at least as many days as had previously produced hypoprothrombinemia by quinine sulphate alone. The vitamin K compound used in this study was a 2-methyl-1,4-naphthoquinone (menaphthone) compound of Glaxo laboratories. The results were interesting as the concurrent administration of vitamin K neutralised the hypoprothrombinemic action of quinine sulphate.

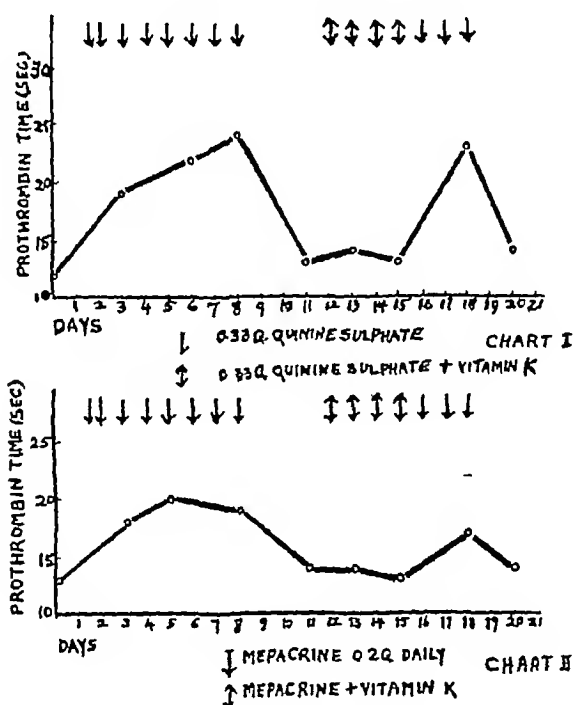


Chart I—Effect of quinine sulphate on prothrombin time and the protective action of vitamin K in P. N., a Hindu male aged 38 years

Chart II—Representative effect of mepacrine on prothrombin time and protective action of vitamin K in M. S., a Hindu male aged 40 years

Next the fourth experimental phase was instituted in which vitamin K was again discontinued and quinine sulphate alone was administered. There was again a rise in the prothrombin time. Quinine hydro-chloride was also tried in one case, besides the above five, and it also had the unquestionable hypoprothrombinemic action.

Chart I portrays the representative effect of quinine sulphate showing the procedure, dosage and results obtained. Table I gives the findings in the five normal subjects.

From Chart I it is clear that quinine definitely produces prothrombopenia, and which can be counteracted by concurrent administration of vitamin K. With the stoppage of vitamin K prothrombin time is again prolonged. The doses of vitamin K used does not indicate its minimum dose required to neutralise the hypoprothrombinemic action of quinine. It was an arbitrary dose used. The minimum dose is yet to be determined.

TABLE I
Effect of Quinine Sulphate on Prothrombin Time in Five Normal Subjects

Case	Age caste sex	Prothrombin time (Seconds)																				
		Normal	0.83 Q S Daily					No Quinine					Q S plus vit. K					Quinine Sulphate				
			Days —1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
P.N	38 H.M	12		18			22		24			18		14		13			28		14	
K.N	28 H.M	15		25			30		30			17		14		12			22		16	
T.R	30 H.B.L	10		18			19		22			12		10		10			20		12	
R.N	28 H.M	14		25			33		31			16		17		17			24		15	
G	35 H.M	14		19			18		20			14		14		13			20		16	

EFFECT OF MEPACRINE ON PROTHROMBIN TIME

Mepacrine is another common anti-malarial drug studied. Its effect on prothrombin time in four normal subjects was studied. It was given in 0.2 g daily doses. The same procedure was adopted as in case of quinine sulphate.

TABLE II
Effect of Mepacrine on Prothrombin Time in Four Normal Subjects

Case	Age Caste Sex	Prothrombin time (seconds)																					
		Normal	Mepacrine 0.2 G Daily					No Mepacrine					Mepacrine & vit K					Mepacrine					
			Days —	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
M.S.	40 H.M.		13		18				20		19			14		14		13			17		14
N.R.	45 H.M.		18		21				22		23			20		18		19			25		16
M.L.	25 H.M.		15		17				18		20			16		16		16			19		15
N.	20 H.M.		13		14				21		22			14		14		18			17		14

From the above findings (Chart II and Table II) it is evident that mepacrine also produces prolongation of the prothrombin time. This hypoprothrombinemia in this case is not as marked as that produced by quinine sulphate. Concurrent administration of vitamin K checks the hypoprothrombinemic action of mepacrine.

ACTION OF QUININE SULPHATE ON PROTHROMBIN TIME IN MALARIAL SUBJECTS

Five cases of malaria were studied. The blood film examination showed the presence of malarial parasites. Prothrombin time before, during and after medication with quinine sulphate was determined.

Case I	Date	B R aged 28 years Medication	Blood film examination showed benign tertian (amoeboid) forms of malarial parasites Prothrombin time.
	10-8-46	Admitted Quinine sulphate 10 grs t. d. s	4 min 20 sec
	11-8-46		
	12-8-46	"	
	13-8-46		1 min 20 sec
	14-8-46	,	
	15-8-46		25 sec
	16-8-46	"	
	17-8-46	10 grs only Quinine stopped	25 sec
	18-8-46	,	
	19-8-46	"	15 sec

The initial prothrombin time was very much prolonged. Under quinine medication, it started coming down, till it became stationary at 25 seconds. With the stoppage of quinine, it came down to 15 seconds.

Case II	Date	R H F aged 80 years Medication	Prothrombin time	
	3-8-46	Admitted Quinine sulphate 5 grs t. d. s	88 sec.	
	4-8-46			
	5-8-46	"	28 sec.	
	6-8-46	"	19 sec	No parasites
	7-8-46	"		
	8-8-46	"	25 sec	
		Quinine stopped		
	9-8-46	,	22 sec	
	10-8-46			
	11-8-46	,		
	12-8-46			
	13-8-46			
	14-8-46			
	15-8-46			
	16-8-46			
	17-8-46			
	18-8-46		14 sec.	

This case is very interesting. The prothrombin time went in decreasing till 6-8-46. The film examination of this date showed the absence of malarial parasites. The quinine was continued and the prothrombin time on the 8th August was again found to be raised. This is comparable to the action of quinine sulphate on normal subjects. The prothrombin time reached normal limits after the quinine was stopped.

Case III	Alfoo M M aged 85 years	Blood film examination showed benign tertian (amoeboid) forms of malarial parasites	
Date	Medication	Prothrombin time	
	Admitted		
24-8-46	Quinine sulphate 5 grs t d s	8 min 28 sec	
25-8-46	"		
26-8-46	"	2 min	
27-8-46	"		
28-8-46			
29-8-46		1 min 15 sec	
30-8-46		82 sec	No parasites
31-8-46			
1-9-46	"	88 sec	
	Quinine stopped		
2-9-46	"		
8-9-46	"	10 sec	

This case again shows that quinine medication brings down prothrombin level to a certain limit which is never normal. It is only after quinine has been stopped that normal figures of prothrombin time are reached.

Case IV	B H M aged 60 years	Blood film examination showed benign tertian (rings and amoeboid) forms of malarial parasites	
	Date	Medication	Prothrombin time
	24-8-46	Admitted Quinine sulphate 5 grs t d s	2 min 29 sec
	25-8-46		
	26-8-46		
	27-8-46		2 min 10 sec
	28-8-46	,	
	29-8-46	,	2 min 55 sec
	30-8-46		
	31-8-46	,	
	1-9-46	5 grs quinine Quinine stopped	No parasites
	2-9-46	,	35 sec

He left the hospital before investigations could be completed. Another estimation after two or three days would have shown the prothrombin time as within normal limits.

Case V	R S H M aged 24 years	Blood film examination showed malignant tertian (crescents) form of malarial parasites		
		Date	Medication	Prothrombin time
		21 9-46	Admitted. Quinine sulphate 10 grs t d s	I min 42 sec
		22 9-46	"	
		23 9-46	"	I min
		24-9-46	"	
		25-9-46	"	80 sec.
		26-9-46	"	80 sec
			Quinine stopped	
		27 9-46	"	
		28 9-46		16 sec

This case also bears out the fact that prothrombin time is very much prolonged as a result of malarial infection. After quinine medication it decreases but never reaches normal limits till quinine is stopped.

COMMENTS

From the above experiments it is evident that quinine produces a definite hypoprothrombinemia which can be corrected by concurrent administration of vitamin K. The results bear out the contention of Pirk and Engelberg (loc cit) that soldiers fighting in the tropics who have been receiving quinine prophylaxis should receive concurrent vitamin K to counteract quinine-induced prothrombinopenia. This combined medication would eliminate the dangers of undue bleeding in these subjects, if they are wounded or operated upon. Mepacrine is also found to prolong the prothrombin time though to a lesser degree.

The problem is not so simple, as malaria itself is reputed to cause haemorrhage (Parry—loc cit). Manson-Bahr (1940) discussing the haemorrhagic forms of malaria, mentions that haemorrhages may occur in almost any organ. The haemorrhagic tendency in malaria is due to marked prolongation of prothrombin time, as is shown by the figures in the following cases determined on the day of admission before quinine medication was started.

Case	Prothrombin time	Type of malaria
R.	88 seconds	Benign tertian
B B	4 min 20 seconds	"
A	8 " 28	"
B	2 " 20	"
S R	8 " 15	Malignant tertian
H	" 38	Benign tertian
R S	1 " 42	Malignant tertian
J	2 " 45	Malignant and benign infection

From these findings it is interesting to note that both the benign and malignant tertian infections produce hypoprothrombinemia and are liable to be complicated with bleeding. Parry's (loc cit) cases were all of malignant tertian infection while the case cited by Laha (loc cit) was one of benign tertian infection.

With these findings, how far are we justified in giving quinine to malarial cases especially with a risk of haemorrhage, when quinine itself is known to produce hypoprothrombinemia? Yet it is an established fact now, that to stop bleeding in malarial cases, administration of quinine is essential (Parry—loc cit, Laha—loc cit). The answer to this query is furnished by the experimental data of the cases quoted in the text. In all these cases, the prothrombin time definitely decreased on the administration of quinine. The decrease occurred to a particular level and then the prothrombin time remained stationary, the patient now being free from fever and the blood films negative for parasites. Further drop occurred to almost within normal limits only after the quinine was stopped.

Is it the cure from malarial infection that reduced prothrombinopenia or is it due to different actions of quinine on prothrombin time in malarial and normal subjects? The answer obviously is the former. Malarial infection produces prothrombinopenia as is evident from the figures of prothrombin time in untreated cases. With the administration of quinine, as the fever and parasites disappear, so the prothrombin time decreases till it reaches almost a stationary figure. This figure represents hypoprothrombinemia pro-

duced by quinine in this subject who is now to be regarded as normal, being free from malaria. If the quinine is now stopped prothrombin time returns to normal limits.

Malarial infection produces hypoprothrombinemia and tendency to haemorrhage. There are no fixed levels of prothrombinopenia at which bleeding is known to be established (Shapiro-1944). As such, the levels to which prothrombin time is reduced as a result of quinine medication, may or may not be a safeguard against bleeding, the combined administration of quinine and vitamin K will reduce the danger of haemorrhagic manifestation in these patients.

SUMMARY

Effects of quinine sulphate and mepacrine on prothrombin time in normal subjects have been studied. These are found to induce hypoprothrombinemia, which can be prevented by concurrent administration of vitamin K.

It is suggested that the troops fighting in the tropics and receiving quinine prophylaxis should be given vitamin K as a routine to check the possibility of prothrombinopenia-induced bleeding from wounds.

Malarial infection is found to produce marked prolongation of prothrombin time, and this accounts for the tendency to haemorrhage in malaria. Treatment by quinine reduces the prothrombinopenia, but the prothrombin time never reaches normal range till vitamin K is also administered concurrently.

Routine administration of vitamin K in conjunction with quinine given for treatment of malaria is also suggested.

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SOME PROBLEMS IN SURGICAL TREATMENT OF GASTRO-DUODENAL ULCER AND THE VALUE OF PARTIAL GASTRECTOMY

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The problem of the treatment of peptic ulcer is an old one. A good amount of literature has been published regarding the treatment of peptic ulcer and if one goes through it, it will be seen that the peptic ulcer at one time was considered a surgical problem and now more recently it has come to be considered a medical problem. When it was considered a surgical problem all cases, irrespective of indication were treated by all sorts of surgical procedures. On the contrary when it came to be considered a medical problem the operations for ulcers were not encouraged but operations for the complications of ulcers increased five-folds with drastic mortality rate. In our opinion, though the peptic ulcer at present is primarily a medical problem, surgery is indicated in case of failure of adequate medical treatment or recurrence after a successful course of medical treatment, and complications supervening on an ulcer.

As far as surgery is concerned, the treatment of peptic ulcer brings up many important problems for consideration. Unlike the disease of the gall bladder and appendix where the disease can be cured by the extirpation of the organ, peptic ulcer cannot be cured, as such an operation is not feasible. So the treatment rests with eradicating or counteracting the cause or causes that give rise to the ulcer. But unfortunately these are not definitely known.

With an idea that an accurate knowledge of aetiological factors would lead to rational line of treatment of peptic ulcer, a number of attempts have been made to produce ulcers experimentally in animals more or less successfully. Mann and Williamson (1923) as well as Macann (1929) amongst others have been able to produce ulcers by artificial methods. Mann and Williamson by their surgical duodenal drainage method shunted the alkaline duodenal secretion in terminal part of the ileum in 16 dogs out of which 14 developed typical jejunal ulcers. Macann on the other hand implanted duodenal cap high up in the fundus of the stomach in animals, 80 per cent of which developed jejunal ulcers, though no appreciable change in acidity of secretion resulted, and he assumed that the jejunal ulcer was due to the failure of neutralisation. Finally Cod and Varco (1940) first reported the intense and sustained effect upon gastric secretion following the injection of Histamine-Bees Wax mixture. Copious secretion of highly acid juice was secreted and the effect lasted for at least 24 hours in majority of cases. Thus for the first time a method became available for producing typical gastric and duodenal ulcers in a variety of intact

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laboratory animals The importance of highly acid gastric juice in the genesis of ulcer was established By these and other experiments it became apparent that two groups of factors play predominant part in the production of the gastro-duodenal ulcers viz,

- (1) Acidity of gastric juice
 - (a) Hyperacidity
 - (b) Inability of bile, pancreatic-juice and succus entericus to neutralise gastric acidity
 - (c) Alteration of normal acid-alkaline mechanism
- (2) Increased susceptibility of mucosa
 - (a) Which may be caused by mechanical, traumatic, bacterial, vascular and nervous factors, or by diathesis, foods, spirits and caffeine
 - (b) Situation—there is progressive increase in susceptibility from duodenum to colon to the gastric juice

It is believed that these two groups of factors must combine to give rise to an ulcer It is well known that gastric hyperacidity can exist without any ulcer and gastro-duodenal ulcers have been known to occur with normal or abnormal acidity But the consensus of opinion is that the acid factor is of much greater importance than that of the susceptibility As far as treatment is concerned it would be the best thing if we could eradicate both the factors viz, hyperactivity and susceptibility The second one is difficult to achieve as it is very indefinite and so we have to rest with the treatment of the first

The operations for counteracting the hyperacidity fall in four groups (1) Operations by which the alkaline juices of the intestine are made to neutralise the gastric acidity (2) Removal of the pyloric mucosa which is supposed to secrete a hormone which stimulates increased acid secretion (3) Removal of a part of the stomach which reduces the acid secreting surface, thus reducing the acidity of the gastric juice (4) Section of the vagi which also reduce the acid secretion Every operation has its own exponents but it is obvious that the operation which brings down the acidity satisfactorily and entails the minimum risk to the patients' life must be preferred

The next problem is the one of selecting the patients for operative treatment It is agreed that all patients having complicated ulcers must be operated The question arises about the non-complicated ulcers In these cases the factors that have bearing on the line of treatment are —(1) The response to the medical treatment (2) The economic status of the patient and (3) The age of the patient It is obvious that when a patient can be cured by medical treatment he ought not be operated upon The patients who are not cured by medical treatment are few However indolent an ulcer may be, it would heal if a proper medical treatment is given for sufficiently long time The difficulty arises in giving a proper treatment and its being continued for a long time even after the ulcer heals otherwise there is likelihood of recurrence of the ulcer

It is all right if the patient can afford prolonged treatment and adjust the life as needed, after the ulcer heals. The difficulty arises in these patients who earn their daily bread and cannot afford a long treatment. The factor of the age is also important. Younger the patient the better is the response to the medical treatment, and those patients can be kept free from the disease for the rest of the life with a little adjustment and in young patient the operative treatment must be deferred. The question of gastric ulcer is different. Here one has always to think of the possibility of malignancy. Moreover the medical treatment is not so effective in these cases. Usually therefore, these cases have to come for operative treatment.

The last and important problem is that of the recurrence of the ulcer. As we have mentioned before, the ulcer is caused by the two factors of the susceptibility and the acidity. In a particular patient it is difficult to say which of the two factors is the dominant one. It is well known that nearly 20 per cent of the duodenal ulcers are met with where there is normal or subnormal gastric acidity, showing at least that in these cases acidity is not the dominant factor. Now all that our treatment, either medical or surgical, does is to bring down the gastric acidity. It is difficult to decide the cause of the susceptibility and usually nothing is done for it. As that cause is still acting in patients who have been operated upon, it is obvious that some of the patients are bound to get a recurrence of the ulcer, does not matter what operation is performed. The other factors that contribute to the recurrence of the ulcer are the amount of reduction in the gastric acidity after the operation and the trauma inflicted during the operative procedure. Obviously therefore that operation which brings down the acidity while inflicting the least trauma should be preferred.

We cannot help making a passing remark to the recent development in the ulcer problem. Certain substances have been isolated from the intestinal mucosa and the urine of the human beings, which show an immunising effect against formation of gastro-duodenal ulcers. Naturally the question arises whether it is a sort of specific disease against which immunity can be acquired. One of those substances called enterogastrone developed by the works of Ivy, Kosaka, Lim, Gray, and Brady in 1937 from the extracts of the mucosa of the small and large intestines has been shown to inhibit the motor and secretory activity of the stomach. In 1943 a substance was developed by Sandweiss, Saltzstein and Farbmann called Anthelone from human urine which has prophylactic, therapeutic and immunising effects without depressing the gastric secretion. A similar substance like enterogastrone has been found in the human urine and is called urogastrone. These works are still in the experimental stage but hold out big possibilities for future development.

The Value of Partial Gastrectomy The two operations mainly performed for gastro-duodenal ulcers are partial gastrectomy and gastro-jejunostomy. The disadvantage of gastro-jejunostomy is that in certain cases the acidity of the gastric juice is not sufficiently neutralised and the patient develops a jejunal ulcer. On

the other hand though the operation of partial gastrectomy definitely reduces acidity in all cases, it also carries a high mortality rate with it

In the K E M Hospital upto 1945 partial gastrectomy was performed in all 33 cases out of which 11 expired, a mortality rate of 33 per cent. A detailed analysis of these cases is appended herewith. On the other hand between 1937-42 gastro-jejunostomy was performed on 45 cases out of which 4 expired, a mortality rate of just above 8 per cent. In our own series of 5 partial gastrectomies the mortality rate was 40 per cent, while that of gastro-jejunostomy was nil. Dr Kaikini performed 173 gastro-jejunostomies for ulcers with a mortality rate of 4 per cent.

Total number of Partial Gastrectomy: 33

Sex: Male — 32

Female — 1

Religion Hindoos 23
 Mohomedans 6
 Christians 4

Gastric Analysis

Hyperacidity 21
Average Max.—78 6 c.c. N/10 HCL
Average Min.—17 2 c.c. N/10 HCL

Anaesthesia —

Spinal 16
General 15 { Ether 13
 Cyclopropane 2

Results

Immediate Cure 22
Expired 11
Average stay in Hospital 33½ days

Follow up —

Only two cases followed
1 One developed ventral hernia later on
2 The other had stroma functioning well after 2 years

<i>Duration of Symptoms:</i>		<i>Average</i> 5½ years
<i>Maximum</i> 12 years	<i>Minimum</i> 6 months	
<i>X Ray findings after Ba meal</i>		
Crater		11
Deformity		15
Pyloric obstruction		2
Gastric ulcer		6
Transposition of viscera		1

Complications:—

<i>Chest Complications</i>	
Haemorrhage	1
Shock	6
Wound infection	8
Burst abdomen	1
Subphrenic abscess	1
Pyrexia	1
No complication in	13

Unfortunately we could not follow up our cases of gastro-jejunostomy to find out the incidence of jejunal ulcers developing after that operation. In Dr Kaikini's series of 173 cases of gastro-jejunostomies there were only two cases of jejunal ulcers. Balfour as well as Walton in their extensive series of gastro-jejunostomies found the incidence of jejunal ulcers at 3 per cent. Department of Surgery of the University of Minnesota recently carried out experiments to evaluate the advantages or otherwise of different operation for gastro-jejunal ulcers. There were 10 per cent of jejunal ulcers after gastro-jejunostomy and none after partial gastrectomy, showing that the latter was more rational.

Now the question arises whether one ought to perform partial gastrectomy because it is more rational or gastro-jejunostomy because it is more safe. By performing a partial gastrectomy we are sure that the patient will not develop a jejunal ulcer if he survives, but his chances of survival, as far as we are concerned, are only 66 per cent. On the other hand if we perform a gastro-jejunostomy his chances of survival are 92 per cent but there is a risk of 10 per cent of his developing a jejunal ulcer later on. The mortality of 8 per cent and morbidity of 10 per cent after gastro-jejunostomy add up to 18 per cent which, we believe, compare favourably to 33 per cent mortality of partial gastrectomy.

It must be borne in mind that the gastro-duodenal ulcer is a disease of otherwise healthy adults who are likely to lead a tolerably good life for many years. To cut this life short in 33 per cent of these cases by doing partial gastrectomy seems unjustifiable to us when we know that 92 per cent of these cases can live a healthy natural life with a doubtful morbidity in 10 per cent of cases. Furthermore we believe that the incidence of jejunal ulcer is much lower in our country than what we find in western countries. This is borne out by Dr Kalkini's figures.

Therefore we believe that in uncomplicated cases of duodenal ulcers only gastro-jejunostomy should be performed and partial gastrectomy should be reserved for only certain complicated duodenal and gastric ulcers, till the time we can bring down the mortality rate of partial gastrectomy to reasonable level.

The reasons for such a high mortality rate for partial gastrectomy are, we think, (1) the poor general condition of our hospital class of patients, (2) faults in technique, and (3) lack of proper pre- and post-operative treatment.

As far as the first is concerned we are helpless. Improvement of general physical condition of a nation, involves a wider question of improvement of the standard of living. As far as technique is concerned we would suggest that we must improve it by experimental surgery on animals. Lack of proper pre-operative treatment also involves the question of funds of the hospital.

Till such time as we master the technique and evaluate the various factors which can cause death, and are able to minimise these factors, we should, for the time being, give up doing partial gastrectomy, on human beings for uncomplicated ulcers. We feel that the factor of importance of human life should not be lost sight of in our zeal to do partial gastrectomy.

DISCUSSION—Dr P. K. Sen was of the opinion that a high mortality alone, should not be a deterrent to our performing partial gastrectomies for the treatment of peptic ulcers. He continued that endeavours to improve the technique should be made rather than give up the operation. This attitude he said would spell disaster to the progress of surgery in this institution.

Dr V. P. Mehta supported the speaker in his plea for improvement in the technique by perfecting it on animals. He quoted Sommerville of the Mayo Clinic who performs the operations of gastro-jejunostomy with ligation of alternate vessels and appendectomy in twenty minutes.

Dr A. V. Baliga said that the speaker had done a great service in bringing the subject for discussion enabling a proper assessment of the factors leading to a high mortality in the operation of partial gastrectomies. He emphasized the need for improvement in the pre-operative and post-operative precautions and a better operation technique.

Dr V. M. Kalkini said "the total number of Gastric operations done by me is 134. Out of these Gastro-jejunostomy was performed in 173 cases of Peptic ulcer including one gastric ulcer. The mortality in these cases was 4%. Gastro-jejunostomy was done on 3 cases of Carcinoma with a mortality of 60%. Gastrectomy was done on seven cases of Carcinoma of the Stomach and all the cases were fatal. Partial Gastrectomy was done in eight cases of duodenal ulcer and all of them recovered. The mortality would have been still lower if the modern pre and post-operative measure like blood transfusion and continuous stomach suction were available. Out of the 173 cases operated on for peptic ulcer (gastro-jejunostomy) only 2 (two) were found to have developed jejunal ulcer.

Gastrectomy is the ideal treatment for a well developed peptic ulcer if medical treatment tried for about six months has been found ineffective especially in the hospital class of patients. According to Winkelstein Sippy feedings do not give any permanent results and may in themselves serve as an added stimulus to the nervous phase of acid secretion.

Dr B. N. Sircar discussed the ways of reducing the mortality by a proper selection of anaesthesia. He added that the use of block anaesthesia combined with a light general anaesthetic and post-operation bronchial suction would be helpful in reducing the mortality. He was of the opinion that anaesthetists should have a share in the observation of the patient during the post-operative period.

Dr M. M. Pandya in replying said that he was gratified to find that the subject evoked the interest of the surgeons and anaesthetists. He hoped that facts however unpleasant, would be faced with courage and a humane spirit.

Dr R N Cooper in concluding said that there was no need for an unduly pessimistic attitude adopted by Dr Pandya. Some of the causes underlying a high mortality figure of 83% were avoidable. He suggested that causes like a shock could be averted by giving a blood transfusion during the course of the operation along with saline and glucose. Pulmonary complications could be averted by post-operative aspiration of the bronchi on the least sign of a pulmonary collapse and a freer use of sulfa drugs and penicillin. A burst abdomen could be prevented by a previous study of serum protein and vitamin levels.

Lahey has stated that the one factor which has helped to reduce his mortality figure was spinal anaesthesia with nupercaine.

He referred to the value of Bees-wax Histamin test for the proper evaluation of the different surgical procedures proposed. He pointed out that the treatment of the duodenal stump was an important matter. Leakage from this end was an important cause in producing a fatality. For his own part he preferred to play for safety and adopted the technique of Sir Hugh Devine and left a sufficient part of the duodenum or even the stomach proximal to the ulcer to ensure sound closure.

Book Reviews and Notices

THE MEDICAL ANNUAL 1946 a Year Book of Treatment and Practitioner's Index
Editor, Sir Henry Tidy and A Randle Short Bristol John Wright & Sons, Ltd 1946
pp 426 44 Art plates Price Rs 11-8-0

This sixty-fourth publication of the world famous medical annual lives upto its usual standard of excellence. It provides in a handy manual abstracts of recent work likely to be of practical use to practitioners, ably edited and critically abstracted by a team of competent British authorities. There is no other single publication in English to compare with this annual. It is a veritable epitome of recent advances in different branches of clinical practice. The practitioner or the post-graduate student who follows it regularly year by year, will find it easy to keep in touch with the progress of scientific medicine.

Critical Notes and Abstracts

THE CLINICAL USE OF ANTICOAGULANTS (E V Allen, Quart Bull NW Univ Med School) Currently, there are two preparations, used clinically, which impair the coagulation of the blood when administered to man, heparin and dicumarol. The disadvantages of the use of the former are its high cost and the need for parenteral administration, the disadvantages of the use of the latter are the need for determination of its effect by a relatively complicated procedure, the delay in effect after administration, and the continuance of effect after administration has been stopped. The disadvantage of the use of both anticoagulants is that haemorrhage may result from the use of them. Advantageous as both heparin and dicumarol are, use of them represents only the first steps in the direction of securing satisfactory anti-coagulants for clinical use.

The effect of Dicumarol on man The chief effect of dicumarol when administered to man is reduction in the prothrombin content of the blood. Whether dicumarol destroys prothrombin or suppresses its formation is unknown to me. The reduction in prothrombin prevents or lessens intravascular thrombosis. There are no other significant effects when administered to man.

The simultaneous use of Heparin and Dicumarol Because the effect of dicumarol is delayed after oral administration heparin must be used when an effect on coagulation of the blood is desired quickly. Heparin is effective within a few minutes but dicumarol may not be effective for twenty-four to forty-eight hours. The usual programme when an effect is needed quickly in the treatment of adults with anti-coagulants is to inject 50 milligrams of heparin intravenously and to administer 300 milligrams of dicumarol by mouth. Heparin in amounts of 50 milligrams is injected intravenously every four hours, until studies of the prothrombin indicate reduction to a satisfactory value (20 per cent).

The administration of dicumarol must be based on the value for prothrombin in the blood. Any other programme may lead to disaster from hemorrhage or to inadequate control of coagulation. Identical amounts may produce widely dissimilar effects on prothrombin when administered to different persons. In our experience at the Mayo Clinic, the Quick method of calculating the value of prothrombin has been found to be entirely reliable. I make a plea for discontinuation of reporting *prothrombin time*. In the interest of uniformity, every laboratory should report the prothrombin, not in seconds but in *percentage of normal*. The problem has been simplified by the observation that the critical figures in treatment with dicumarol are those representing 10 per cent, 20 per cent, and 30 per cent of normal prothrombin. One may administer dicumarol adequately knowing only these figures, for clinical experience has indicated that intravascular thrombosis rarely occurs when the percentage prothrombin in the blood is less than 30, and bleeding rarely occurs when the percentage prothrombin is 10 or more.

Three hundred milligrams of dicumarol are given on the first day and 200 milligrams are given on the second day. On each subsequent day of therapy the percentage prothrombin is determined and reported. If the value is more than 20 per cent 200 milligrams are given, if it is less than 20 per cent none is given. There are minor exceptions to this programme. If the patient's blood is sensitive to the effect of dicumarol, only 100 mgm may be given, instead of 200 mgm. If the patient's blood is insensitive to the effect of dicumarol, 300 mgm may be given instead of 200 mgm. If the percentage prothrombin is decreasing rapidly but is more than 20, no dicumarol is given. If it is rising rapidly, but has not yet quite reached 20 per cent, the drug is given on that day. Ordinarily treatment with dicumarol is continued until the patient has been ambulatory for about one week.

Control of excessive prothrombin deficiency and induced haemorrhage It was originally believed that Vitamin K was ineffective in correcting prothrombin deficiency induced by dicumarol. It is now known that the amounts of vitamin K which were used were entirely inadequate and that 64 mgm of menadione bisulfite (injected intravenously) corrects excessive prothrombin deficiencies in the great majority of patients. Transfusion of 500 c.c. of blood, preferably fresh, is also effective, it may need to be given once or twice daily until bleeding stops. If an emergency operation must be performed on a patient who is receiving heparin discontinuation for an hour or so will permit the blood to return to a normal state of coagulability. If an emergency operation must be performed on a patient receiving dicumarol, large amounts of vitamin K, and transfusions may be given to return the percentage of prothrombin toward normal values.

Indications for Anti coagulant Therapy 1 After non-fatal pulmonary embolism to prevent further embolism which may be fatal

2 For thrombophlebitis and phlebothrombosis to prevent further venous thrombosis and pulmonary embolism

3 For sudden arterial occlusion (embolism and thrombosis) to prevent arterial thrombosis which results from ischemia of intima (distal to the area of occlusion) and to prevent thrombosis of an artery at the site of embolectomy provided a surgeon removes the embolus

4 Traumatic injury to blood vessels to avoid thrombosis

Possible Indications for Anti coagulant Therapy 1 Prophylaxis against post-operative venous thrombosis (dicumarol only) in cases of previous venous thrombosis or embolism

2 After abdominal hysterectomy (dicumarol only) because 4 per cent of patients who have this operation have post-operative venous thrombosis or embolism and 0.7 per cent die of fatal embolism

3 In myocardial infarction, congestive heart failure and cardiac irregularities which predispose to embolism

4 Older patients who are confined to bed for long periods (dicumarol only)

Conditions in which anti-coagulants are to be used cautiously or not at all 1 Vitamin C and K deficiencies or profound liver disease with prothrombin deficiency

2 In renal insufficiency

3 In blood dyscrasias with impairment of the normal coagulation mechanism

4 Recent operations on the brain or spinal cord

5 Ulcerative lesions or open wounds

Anti-coagulant Versus Ligation of Veins When venous thrombosis has occurred, treatment is required for two purposes, to prevent further thrombosis and to prevent pulmonary embolism. There are two currently competitive programs of treatment, ligation of veins and the use of the anti-coagulants, heparin and dicumarol. Neither program of treatment is generally considered superior to the other, although each has its proponents who see a little virtue in the other. The proponents of venous ligation believe that this simple method interrupting continuity of a vein prevents the transportation of a clot by the blood. That is true for the single vein which is ligated. Those who see less virtue in ligation of veins believe that thrombi may originate in other veins and thus cause pulmonary embolism, indeed the figures on venous ligation indicate that this is true. Nonetheless, this operative procedure has definite value. However, ligation of veins does not stop venous thrombosis, it simply prevents pulmonary embolism from originating in the distal part of the ligated vein. Ligation of the inferior vena cava is admittedly an effective measure but the question relative to the advisability and necessity of such a "major" procedure has not been satisfactorily answered. Disaster may even follow ligation of the femoral vein for venous thrombosis. The proponents of the use of anti-coagulants believe that all that can be accomplished by ligation of veins can be accomplished by anti-coagulants. The sole danger from use of anti-coagulants reduces the danger of bleeding to an almost insignificant minimum. Where less expertness and knowledge are exercised the danger may be great.

A NEW ANTI-MALARIAL AGENT CHLOROQUINE (SN 7618) has been compared to quinacrine as an anti-malarial agent. It has proved effective in the suppression of malaria and in the treatment of an acute attack of this disease. Data on the pharmacologic, toxicologic and anti-malarial actions of this new substance are presented.

Absorption, excretion, tissue distribution and degradation The absorption of SN 7618 from the gastro-intestinal tract, like that of quinacrine, is complete or nearly complete. SN 7618 is absorbed somewhat more rapidly than quinacrine and, because of lesser localisation, is present in substantially high concentrations than quinacrine on any given dosage schedule. Excretion of SN 7618 is slow but is slightly more rapid than that of quinacrine. The urinary output of SN 7618 may be increased by acidification of the urine and decreased by alkalization.

Considerable amounts of SN 7618 are deposited in the organs and tissues, the quantities being proportional to the dose of the drug.

SN 7618 is concentrated in nucleated cells, especially those of the liver, spleen, kidneys and lung. These organs contain the highest concentrations, from 200 to 500 times the amount in plasma. The drug is also concentrated to a considerable extent in leucocytes. Brain and spinal cord contain the lowest concentration, no more than 10 to 25 times the amount in plasma. Thus, the general pattern of distribution of SN 7618 is similar to that of quinacrine.

SN 7618, like quinacrine, is metabolised in the body, only a small part of the drug administered being found in the excreta. Ten to 20 per cent is excreted unchanged in the urine and, as noted, the latter fraction can be increased by acidification of the urine. The definite localisation of SN 7618 in the organs with the slow rate of excretion and degradation necessitates the administration of a priming dose if the desired concentration of drug in the plasma is to be rapidly reached and maintained. As in the case of quinacrine, these factors result in a slow disappearance of SN 7618 from the body when the dosage is discontinued, the concentration of the drug in the body fluids generally falls about 60 per cent per week when drug administration is stopped.

Toxicity There is little difference in the toxicity of SN 7618 and that of quinacrine in experimental animals. In man, the symptoms which have been observed following doses of SN 7618 adequate for treatment of the acute attack include mild and transient headache, visual disturbances, pruritus and gastro-intestinal complaints. In chronic toxicity studies in man using a dose (0.5 gm weekly) in excess of that necessary for adequate suppression, no serious symptoms and no impairment of health have been observed in 31 subjects over a period of eleven months of consecutive drug administration. In studying the record of about 5,000 individuals who have received SN 7618, every symptom which has been observed has been recorded in an effort to bring out even minimal toxic manifestations. In a small number of instances, usually with doses higher than necessary for either treatment or suppression, individual subjects have refused to continue drug administration because of unpleasant symptoms. None of these manifestations has been constitutionally serious and all have been readily reversible. Unlike quinacrine, SN 7618 does not discolour the skin.

In a study of the chronic toxicity of SN 7618 on a dosage of 0.5 gm once a week, 1 patient in 31 after eight months developed a lichen planus-like eruption. This eruption subsided ten days after discontinuation of the drug.

Anti-malarial activity SN 7618 is more active than quinacrine in all the avian malarias in which it has been tested. SN 7618 is highly active against the erythrocytic forms of *P. vivax* and *P. falciparum*. It does not prevent relapses in vivax malaria even when administered in doses many times those required to terminate an acute attack, nor will it prevent the establishment of vivax infection when administered as a prophylactic. It is highly effective in vivax malaria as a suppressive agent and in the termination of acute attacks, significantly lengthening the interval between

treatment and relapse beyond that observed with quinacrine or quinine. In falciparum malaria it has been demonstrated to suppress the acute attack and to effect complete cure of the infection. Studies of the anti-malarial activity of SN 7618 against well standardised strains of *P. vivax* and *P. falciparum* have shown its activity to be approximately three times that of quinacrine. In well tolerated therapeutic doses a great majority of patients will be afebrile within 24 hours and the remainder within 48 hours. Thick smears for parasites will generally be negative at 48 to 72 hours.

Recommended dosage regimens. In suppression Effective suppression of malaria with single weekly doses has been demonstrated. For suppressive therapy a dose of 0.3 gm given on the same day each week is recommended. In treatment of the acute attack An initial dose of 0.6 gm. of SN 7618 followed by an additional 0.3 gm after 6 to 8 hours and a single dose of 0.3 gm on each of two consecutive days is sufficient to produce prompt disappearance of symptoms and parasitemia. This regimen eradicates infection due to *P. falciparum* and terminates the acute attack of *P. vivax* infection. In the latter, freedom from clinical attacks may be maintained thereafter by administration of suppressive doses as recommended. Satisfactory responses have also been reported following the administration of 1.2 gm in divided doses over a period of 24 hours (J.A.M.A. April 20, 1946, 130: 1069).

Clinical Case Reports

WEIL'S DISEASE Leptospirosis icterohaemorrhagica treated with Penicillin—N. D. PATEL, M.D. (Lond.), M.R.C.P. (Lond.)

N. K., a Hindu youth of seventeen years (K. E. M. Hospital Reg. No. 91585) was admitted on Sept. 22, 1946 because of severe bleeding from the nose for one day, fever and pain in the abdomen for four days. He was a tailor by occupation and was living in Parel, Bombay. There was no history of occupational, accidental or intentional immersion in polluted water.

On physical examination the patient was found to be poorly nourished, drowsy, restless and apparently too ill for the temperature, which was only 99.8°F. The pulse rate, however, was rapid, 112 per minute and respiration 30 per minute. There was bleeding from both nostrils, gums, and he had an occasional cough with blood-tinged expectoration. The skin and mucous membranes were not icteric, nor was there any rash. In the lungs no abnormal signs could be discovered. The heart was normal, BP 105/60 mm of mercury. The abdominal wall was tender on palpation. Liver or spleen could not be felt. The central nervous system was normal. All muscles of the body were tender on deep pressure. The urine showed a trace of albumin but no red blood cells or bile.

The next day, Sept, 23, 5th day of disease, the patient showed a slight icteric tinge of the conjunctiva and vomited a little blood. The epistaxis and bleeding from the gums continued. The urine showed a little bile. Though the temperature was normal 98°F the pulse and respiration rates were 130 and 30. The blood showed 65 per cent haemoglobin with 3,500,000 red blood corpuscles and 30,000 white blood corpuscles with 72 per cent PMN, 26 per cent lymphocytes and 2 per cent monocytes. The patient continued in the same toxic condition, daily feeling and looking worse, till Sept, 27, though the temperature did not go above 99°F. The jaundice was now getting deeper, the icteric index being 120, and van den Bergh direct immediate positive. On the 27th, i.e., on the 9th day of disease a maculo-papular rash appeared on the trunk. The bleeding from the nose stopped. There was a suspicion of an enlarged spleen. On the 28th there appeared profuse petechial haemorrhages all over the body. There were also a few purpuric patches. The stools were never tarry or bloody. Blood was sent on Sept, 30, for agglutination test for leptospira ictero-haemorrhagica which was reported on Oct, 2, to be positive in a dilution of 1/160 only. Though there was no temperature, the patient became very toxic, semistuporose and deeply jaundiced. Though it was desirable to investigate the renal function, it was not possible. Up to now the treatment was symptomatic with injections of glucose, calcium and saline. On Oct, 2 the patient was put on penicillin injections 50,000 units 3 hourly. Within 24 hours the temperature began to rise (102°F), after 48 hours the dose was reduced to 30,000 units 3 hourly, and was continued till Oct, 20. The patient began to feel and look better, and the rash began to get darker and faded away by Oct, 7. This was followed by brawny desquamation of the skin of the face and trunk. The temperature ranged between 99° and 104°F and persisted up to Oct, 17, 30th day of the disease. The blood sent on Oct, 14, agglutinated a suspension of leptospira ictero-haemorrhagica in a dilution of 1 in 6400. Jaundice persisted up to Oct, 24.

The general condition of the patient improved remarkably though the anaemia increased (RBC fell to 2,400,000, and Hb to 58 per cent) and there appeared some oedema of the legs. He was put on large doses of iron and injections of protein hydrolysate 200 c.c. i.v. on alternate days. He made a complete clinical recovery and was discharged on Nov 9.

Leptospirosis ictero-haemorrhagica (Weil's disease) is common in Bombay. The organism is susceptible to penicillin. The disease, though varies in severity, has a high mortality. An early diagnosis and specific treatment are imperative. All teaching institutions and public hospitals must provide facilities for early diagnosis (guinea pig inoculation, dark-field examination for spirochetes, agglutination tests, renal function tests and muscle biopsy,) and treatment with penicillin, which must be instituted at the earliest suspicion of the disease in a patient with fever and marked prostration (2 to 9 days) in the septicemic stage and with jaundice and renal failure (10th to 20th day) in the icteric and uremic stage. Clinical

diagnosis before jaundice appears is rarely possible. Necrosis of isolated muscle fibres or of a small portion of the fibre, in the voluntary muscles, particularly of the leg, is said to be a characteristic lesion, constant enough to serve as an accurate means of diagnosis by muscle biopsy.

Reflections and Aphorisms

In cases of neurosyphilis there are *four tests* which are of especial significance in the routine examination of the cerebrospinal fluid: (1) the cell count, (2) estimation of the protein content (qualitative and quantitative test), (3) colloidal tests, and (4) specific complement fixation, precipitation, or flocculation tests.

Lumbar puncture should be performed *only* after the patient has been *thoroughly* examined and it has been determined *what information is desired from the puncture*.

In reading the pressure of the CSF, allow at least five minutes for the patient to get completely relaxed, otherwise false high values are likely to be obtained.

The dynamics of the CSF should be studied both by the jugular and the abdominal compression.

To prevent untoward accidents, in case of an elevated CSF pressure, the fluid should be removed slowly, in small amounts, and the pressure should not be allowed to fall under one-half its original level. 2151

Gumma of the central nervous system is a clinical rarity. Chronic gummatous basal meningitis is a different affair.

The number of cells (normally less than 5 c.mm.) in the CSF roughly represents the degree of meningeal reaction. Occasionally in late or burnt-out stages of neuro-syphilis, the cell count may be low, less than 10 per c.mm.

Before ordering a Wassermann reaction remember that innumerable unnecessary blood examinations are carried out, because the clinical observer too often and prematurely passes *his* diagnostic problems to the clinical pathologist, when it is *his* primary function to exhaust the possibilities of clinical observation before he asks the pathologist to carry him on his back.

The total protein (normally less than 50 mgm per 100 cc) content is increased in all cases of acute and chronic inflammation of the meninges, in certain degenerative diseases of the nervous system, in most tumors of the brain, in all tumors of the spinal cord or in lesions producing sub-arachnoidal block, and in occasional cases of polyneuritis.

The normal albumin globulin ratio in CSF is 4 to 1. In syphilis of the nervous system the globulin fraction is often increased to a greater degree than the albumin fraction. Specific tests for detecting the relative increase in globulin are of great diagnostic value.

The mechanism of the production of the colour change and precipitation has never been clearly understood. It is suggested

that it may be due to a disturbance of the albumin-globulin ratio of the fluid

The first-zone curve, commonly called the paretic curve, is not pathognomonic of the dementia paralytica. Though it is almost constantly present in untreated cases of GPI, it is frequently found in other forms of neurosyphilis and in non-syphilitic diseases, such as purulent meningitis, tubercular meningitis, acute encephalomyelitis, brain tumor or abscess, aseptic meningeal reaction, disseminate sclerosis, polyneuritis and in bloody fluids from cases with cerebral haemorrhage.

A decrease in the sugar content of the spinal fluid is, with rare exceptions, indicative of an infection of the meninges due to a local breakdown of sugar by pathogenic micro-organisms. An increase in the sugar content of the fluid is indicative only of a high blood sugar.

A normal spinal fluid in adequately treated cases of early syphilis 2 years after infection will remain normal and a normal fluid in a treated or untreated case with no clinical evidence of neurosyphilis 4 years after the infection, is a practical guarantee against subsequent development of severe nervous damage.

The diagnosis of paretic neurosyphilis in an untreated patient is practically never justified in the absence of the "Paretic Formula", which is (1) a clear fluid under a normal or slightly increased pressure, (2) a pleocytosis varying from 25 to 75 cells per c.mm., (3) a positive globulin test and an increased total protein content, usually between 50 and 100 mg per 100 cc., (4) a first-zone colloidal gold reaction, and (5) a strongly positive Wassermann reaction.

In the absence of this formula GPI should never be diagnosed, but its presence is not in itself diagnostic of paretic neurosyphilis, since these changes may be present in patients, with tabetic, meningeal, vascular, or asymptomatic neurosyphilis.

There is no way of foretelling at the time of original infection whether neurosyphilis will develop in a given case or which form it will assume. *Febrile diseases, pregnancy, and race* are the known factors which reduce the incidence of clinical neurosyphilis.

At present there is no clear cut experimental evidence available suggesting the advisability of the use of any particular arsphenamine product in neurosyphilis, one must depend largely on clinical impressions. Penicillin appears to be an active therapeutic agent in all forms of neurosyphilis. Perhaps the best clinical results are likely to be obtained from a combination of penicillin with therapeutic fever, followed by courses of trivalent or pentavalent arsenic and bismuth.

CLAIMS OF AYURVEDA

"Let us consider the claims of Ayurveda, Hindu system of medicine. It is said by scholars of comparative medicine and history that it had started well with anatomy. But its anatomy was imperfect, lacking in essential details, and when it came to physiology and pathology, these were not so much founded on observational facts but on certain philosophical concepts. The Tridhatu Sidhanta is an attempt to visualise the organism as microcosmos, and to place it in relationship with the macrocosmos of the universe. Though Ayurveda is thus mainly philosophic in its outlook, and its physiology and pathology mainly speculative in conception, it had attained, as judged from the purely empirical standard of the pre-scientific era, a high standard of excellence in medicine including surgery. Diseases were studied mainly by observation of a few symptoms and signs, depending mainly on mother wit and shrewd intuition. There was very little apparatus to aid their observations. Despite all these drawbacks, it must be said that the success and extent of medical treatment in ancient India were higher than in any other country. The Ayurvedic medicine is said to have reached its zenith in the Buddhist period. Then there was a gradual decline and retrogression ever since.

In this day of veritable Indian renaissance when an effort is made to revive all our ancient culture and arts, it is but natural to desire to resuscitate the ancient systems of medicine also. Attempts have been set on foot for some years already towards this end. Amongst the active protagonists there are two schools of thought. There are those, firstly, who claim that Ayurveda is self-contained and self-sufficient according to its own postulates of physiology and pathology and is capable of being worked as an effective system of medicine. It does not admit of any additions or improvement without violating its basic principles and theory. If we should accept this view, we must put the future student of medicine to a study of the ancient classics like Charaka and Susruta and after such a course of study he will be qualified to practise medicine on the lines laid down in the ancient classics. But, he will be practising a system of medicine to which are denied and tabooed all the recent scientific advances of modern medicine, diagnostic as well as therapeutic. He practises a system of medicine based upon concepts of anatomy, physiology and pathology which were conceived centuries ago and whose reality has come to be questioned at the hands of modern science, one wonders, if any government will be so bold as to offer this to its people, as an effective system of medicine, in spite of all the aforesaid defects and to hope to grapple with the complex problems of health, in the modern times.

Secondly, there is a different set of people who while realising the out-of-date nature and the consequent inadequacy of the indigenous medicine yet believe that it could be made the basis of

study, and that its inaccuracies and inadequacies duly corrected and made up by patching it up, with an item here and there from the modern medicine. This is the experiment that has been tried for the last two decades in the Madras School of Indian Medicine. People who have observed this experiment at close quarters say, *that it has proved a thorough failure*. It has been said that the students are trained half in the Indian and half in the western medicine, *in a hotch-potch of both systems*. The result is, *it has produced a set of practitioners who are ill-equipped and ill-trained at the end*. Thus the experiment has not only failed to resuscitate ancient medicine but also showed it is not likely to succeed. The pundits who have been in charge of conducting this experiment, do not seem to have even attempted to evolve any formula or working hypothesis, for the synthesis or harmonious combination of both systems of medicine, though this experiment itself was originally started with this avowed aim and object.

It is highly debatable that the ancient Hindu medicine, *old and decadant, static in conception and practice, having lost its genius to absorb and assimilate fresh facts and ideas, can ever be revived as a living system of medicine*. It is a fond hope that it is capable of making modern medicine part and parcel of it as it did in the case of Arabic medicine some centuries back while it was still full of life and growth. The same is the fear with regard to Unani system also. We must also bear in mind that these ancient systems of medicine are *remedial and individualistic* in their application. As a means of assuaging pain and relieving suffering, they made, no doubt, a powerful appeal to the feelings of men. But the rapid strides of progress that modern medical science has made, have become remarkable not only for the precision and accuracy of *diagnosis, and treatment*, but also have given birth to the movement of *preventive medicine and public health*. More recently comest the gospel of *positive health or wholeness of body and mind*, it is based upon a positive conception of health. It is not a study of mere absence of detectable diseases nor is it satisfied with mere prevention of disease. It aims at reaching and maintaining the optimum bodily and mental development and integrity, individual as well as communal. It involves an investigation and study of the social and environmental factors which promote ill health and disability and adopt such measures as contribute to the full development and functional activity of men, both physical and mental. The biblical saying that "they that are whole need not a physician but they that are sick" does not seem to hold good any longer, for the mission of medical man in modern economic and social conditions, is more comprehensive than mere treatment of disease or injury. It includes also the education, preservation, protection, and promotion of health, individual as well as communal. Such is the aim and purpose of modern scientific medicine one wonders whether *any other system* of medicine, either ancient or modern, is so comprehensive in its conception and application of its methods."

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Original Contributions

UNUSUAL CHANGES IN FIBRO-ADENOMA OF THE BREAST*

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The breast like the endometrium is constantly undergoing periodic changes of hyperplasia and involution and it is regulated by the internal secretions of the ovary. The periacinous and periductal connective tissue is under the influence of follicular and the interstitial tissue of the ovary. While the duct and acinus epithelium is under the control of the corpus luteum. If this control becomes abnormal the periodic mammary changes may cross the borderline from physiologic into the pathologic state. During the first decade of the menstrual life the common pathologic change that occurs in the breast is a fibro-adenoma.

Fibro-adenomas occur in men but are extremely rare. They rarely develop before puberty. They may be multiple in one breast but rarely bilateral. They are rarely associated with pain which is usually increased during menstrual periods. Between puberty and the age of twenty-five fibro-adenoma is the most common tumour of the female breast. It appears as firm, solid, round or lobulated mass which is freely movable, apparently circumscribed, but not actually encapsulated. It does not adhere to the skin and does not cause retraction of the nipple. A sudden or rapid increase in growth may occur as a result of pregnancy. Such lactating tumours may grow to large proportions. A vague discomfort localised to the site of the tumour is more common. These tumours must be differentiated from cysts and from carcinomas. Two events may complicate the course of fibro-adenoma of the breast. The tumours may increase in size or they may undergo a malignant change.² Geschikter³ gives three reasons for a prompt excision of benign fibro-adenoma at the time of clinical recognition.

1 To establish diagnosis

2 To avoid mutilating operations for large tumours that result from rapid growth during pregnancy, or at the menopause

3 To prevent a malignant change at periods of rapid growth. During gestation and lactation the fibro-adenoma may grow rapidly as a result of hormonal influences of gestation or lactation.

* A study under Dr V R Khanolkar, B.Sc., M.D. (Lond.), Director of Laboratories.

The variety of microscopical changes thus brought about may lead to difficulties in diagnosis and as a result the patient may be subjected to unnecessary major operations

The microscopic changes occurring in a fibro-adenoma during pregnancy roughly correspond to those occurring in the surrounding normal mammary tissue. The changes in the tumour however are pronounced at the margins. Tumours of long standing, with hyalinised connective tissue stroma may however remain refractory to pregnancy changes. Those which have responded to the previous pregnancy may remain unchanged during subsequent gestation ^{4 & 6}

During the last five years 451 tumours of the breast were studied in the laboratories of the Tata Memorial Hospital. The classification of these is as follows

Benign	Fibroadenoma	53
	Papilloma	12
	Lipoma	2
	Myoepithelial tumour	1
Malignant	Carcinoma	370
	Sarcoma	7
Total		451

Out of the 53 cases of fibro-adenomas, the following five cases may interest the clinician as they present some unusual features

A surgeon is cautious while dealing with tumours of the breast to be certain of the diagnosis regarding malignancy before he undertakes a radical operative measure. He is, therefore, keen for a diagnosis being made by frozen section technique, rather than depending fully on his clinical acumen. Much useful information is obtained by a pathologist by naked eye inspection of the resected tissue and as a rule it is not difficult to recognise the nature of the lesion. The carcinoma, fibro-adenoma and chronic cystic mastitis have specific macroscopic and microscopic appearances. It is however necessary to be familiar with certain unusual changes which occur in a fibro-adenoma else a mistaken diagnosis may subject a patient to unnecessary radical operative procedure. The following first two cases are those where fibro-adenoma showed changes during gestation and lactation. The importance of recognition of changes in fibro-adenoma during the period of gestation or lactation is in a correct diagnosis. The dilated and compact acini may lead to a mistaken diagnosis of a Comedo-Carcinoma. The two other cases are those where carcinomatous and sarcomatous changes were seen in a fibro-adenoma. The fifth case is interesting since cartilaginous changes occurring in the human breast is extremely rare.

Case 1 1050 A female patient aged 30 years was admitted to the hospital on 29-9-41. She was married 3 years ago and had one pregnancy 11 months ago. 10 months ago she noticed a lump in the left breast which has been painless. On clinical examination the breasts were symmetrical and not particularly tender. In the left breast in the upper and outer quadrant was a movable lump 2.5 cms

in diameter attached to the overlying skin (Fig 1) The axillary lymph nodes were not palpable A clinical diagnosis of fibro-adenoma in lactating breast was made and the patient was called again after two months for evaluation After a period of two months it was found that the mass which was attached to the overlying skin was larger It measured 4 cms in diameter and that there were soft palpable nodes in the axilla The patient was admitted to the hospital and under local anaesthesia excision of the lump was done On frozen section examination the excised tumour was found to be a fibro-adenoma showing changes due to lactation

Gross observations of the Specimen A specimen of simple mastectomy measuring 8 x 8 x 3 cms There was a small localised growth measuring 4 x 3 x 3 cms (Fig 2) On cutting into the localised growth a whitish milk like fluid exuded out The cut surface looked cystic and on squeezing, fragments of cheesy material came out readily

Microscopical examination The sections showed areas of intracanalicular fibro-adenoma The ducts and acini at the periphery of the neoplasm were seen enclosing luminae of different sizes and shapes (Fig 3) Some of these luminae were filled in with macrophage cells Section through the breast parenchyma showed changes usually seen in the lactating breast

Case 2 (F 1180) A female patient aged 19 years first noticed a nodule in the left breast a year ago It gradually increased in size and at the birth of the first child it increased still more rapidly It caused no pain During operation a cyst was seen embedded in breast parenchyma from which large amount of thick inspissated material exuded out when it was accidentally punctured

Gross observations of the Specimen It was a growth enclosing a thick wall cyst Adjacent to this was seen an ovoid firm nodule measuring 2 cms in long axis (Fig 4) It showed greyish and rather dense areas but the whorls could not be discovered The encapsulation of the nodule suggested it to be a fibro-adenoma

Microscopical examination The section through the wall of the cyst showed desquamated epithelium and sheets of macrophage cells The outer layer showed compressed connective tissues The section through the small nodule (fibro-adenoma) showed dilated ducts and acini closely packed together These were lined by a single layer of cuboidal epithelium (Fig 5) The nuclei were mostly round in shape and uniform in size The cytoplasm was faintly basophilic and showed many vacuoles The changes mostly resembled those seen in the small resected portion of the breast parenchyma

Warren⁸ is of opinion that women with previous history of an excision of a fibro-adenoma are twice as susceptible to cancer of the breast as normal women of same age group Geschickter and Copeland followed 201 such patients for a period ranging from 1-10 years and found breast cancer in 2 cases There is yet an interesting observation seen in experimental animals For instance in rats developing fibro-adenoma of breast in response to estrogen it was

found that if the stimulation was maintained by estrogen over periods exceeding 1 year almost half the number of animals developed cancer

Case 3 5615 A 41 year old woman who has been married for 28 years and had 3 children complained of a lump in the right breast. She noticed it 7 months previously. It was a small nodule to start with which gradually increased in size. On clinical examination a hard regular lump about 6 cms in diameter was felt beneath the nipple. It was movable on the chest wall. There was no discharge through the nipple. The axillary lymph nodes were palpable. The liver was slightly palpable and there was a soft systolic murmur in the mitral area.

Gross Observation of the Specimen A specimen of simple mastectomy with an elliptical skin flap measuring $15\frac{1}{2} \times 11$ cms. The nipple was intact and not retracted. On cut section was seen a hard tumour measuring 6 cms in its long axis. It showed streaks and chalky points as are often associated with cancerous condition. But enclosed within the tumour mass and adjacent to the fascia and the muscle was a circular encapsulated growth $1\frac{1}{2}$ cms in diameter showing a whorled area, presenting a naked eye appearance of a fibro-adenoma (Fig 6). There was a considerable amount of adipose tissue surrounding the tumour. The breast parenchyma showed glandular atrophy.

Microscopical Examination The sections through the tumour area showed sheets and strands of polygonal cells. The cytoplasm of the tumour cells was faintly basophilic. The nuclei were hyperchromatic and showed a prominent nucleolus. There was a marked variation in size and shape of the nuclei. The neoplastic cells showed moderate tendency to formation of acini. Frequent mitosis could be seen. The examination of the section through the whorled area (gross) presented very interesting histological features. The acini and ducts were either orderly or distorted tubular structures which were surrounded by dense hyalinised strands of connective tissue. The cells lining the acini showed atypical proliferation. The nuclear characters in these were distinctly malignant as could be seen in the microphotograph (Fig 7). The nuclei were hyperchromatic and showed a variation in size and shape. This suggested that the carcinoma had probably originated in the epithelium of a benign tumour?

It is generally recognised that a large number of sarcomas of breast arise in pre-existing fibro-adenoma. Deaver and McFarland stated that in a total of 838 sarcomas in the breast, 193 were adenocarcinomas, probably arising out of a sarcomatous transformation in a fibro-adenoma. They were of opinion that 193 cases of adenocarcinoma that they described superimposed on fibro-adenoma. It may be interesting to co-relate this with results obtained from animal experimentation. Helman in studying benign neoplasms of the breast of the rat found that after 26 successive transplantations of spontaneous fibro-adenoma the tumour suddenly became sarcomatous. Such an observation is also important in view of published

SIRSAT

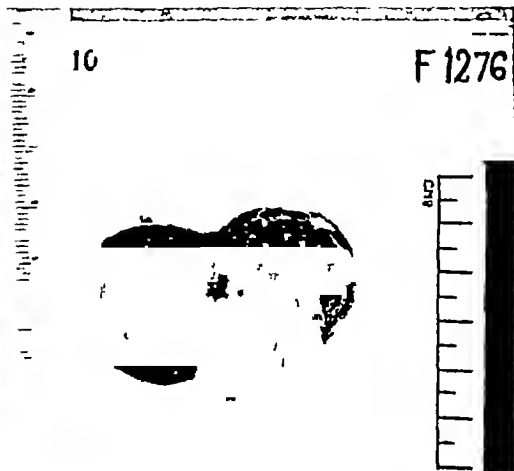
Fig. 1

Fig. 2

Fig 10



A 1303



F 1180



6

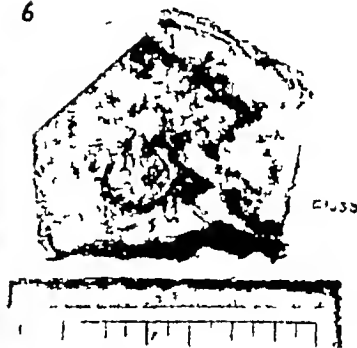


Fig 4

Fig 6

Fig 1 Case 1 (1050) Patient with a fibro adenoma in a lactating breast

Fig 2 Case 1 (A 1303) Specimen showing an encapsulated tumour with multiple cysts of varying sizes

Fig 4 Case 2 (F 1180) An ovoid fibro adenoma approximately 2 cms in its long axis

Fig 6 Case 3 (C 1350) Specimen of fibro adenoma showing a typical proliferation of cells lining the ducts acini (see fig 7)

Fig 10 Case 5 A fibro adenoma showing in the centre an area presenting cartilaginous appearance (see fig

Fig 8

Fig 5



Fig 9

Fig 11

Fig 3 Case 1 Section through the tumour (Fig 2) showing distorted acini and ducts. Note at the periphery dilated ducts and acini.

Fig 5 Case 2 Section through the fibroadenoma (fig 4). Note dilated ducts and acini lined by a single layer of cuboidal epithelium. Note the vacuolated cytoplasm.

Fig 7 Case 3 Dilated ducts and acini showing atypical proliferation of the lining cell. (Section through the fibroadenoma fig 6). Tumour surrounding this shows structure of an anaplastic carcinoma (not seen in photomicrograph).

Fig 8 Case 4 Distorted ducts and acini of the mammary gland. The stroma shows atypical proliferation of the cells.

Fig 9 Case 4 (High power photomicrograph). Note the stroma cells. These are hyperchromatic and show a marked variation in size. Mononuclear giant cells are seen.

Fig 11 Section through the cartilage area in (fig 10). Note the cartilage cells. At the periphery are seen dilated and tubular acini and ducts of the mammary gland presenting a typical appearance of a pericanalicular fibroadenoma (not seen in photomicrograph).

reports of slowly growing human breast tumours suddenly changing their nature and assuming clinical and morphological attributes of a sarcoma⁵

Case 4 (D 950) A female patient aged 54 noticed a lump in the right breast which was not attached to the skin or fascia. The axillary lymph nodes were not palpable. It was clinically diagnosed as a case of carcinoma of the breast and the surgeon preferred to do the radical mastectomy.

Gross observations of the Specimen It was an ovoid gelatinous mass embedded in adipose tissue. It measured 3 cms in its long axis. It was firm to feel and showed glistening greyish stroma which was seen arranged in whorls.

Microscopical Examination It showed tubular or distorted mammary acini surrounded by strands of connective tissue. The acini were lined by a single layer of cuboidal epithelium. The surrounding strands of tissue showed atypical characteristics of the nuclei such as multinucleated giant cells, atypical mitosis and hyperchromatism (Figs 8 and 9). These changes which were of a malignant nature were localised to the surrounding stroma. On the basis of this a diagnosis of a fibro-adenoma of the breast showing sarcomatous changes in connective tissue stroma was made.

Cheate and Cutler¹ have reported small chondromatous nodules in two cases of fibro-adenoma. In one case a cartilaginous nodule measured 2 cms in diameter and occurred in a fibro-adenoma of long standing. In another case cartilage and bone formation were both present in a small nodule of intracanalicular fibro-adenoma in the breast of a woman 57 years old.

Case 5 (F 1276) A female patient aged 35 years gave a history of a lump in the breast. She had first noticed it 10 years prior to admission. The mass had been increasing recently. On clinical examination a lump was felt in the upper and outer quadrant of the right breast. It was freely movable. A clinical diagnosis of fibro-adenoma of the breast was made and the lump was excised.

Gross observations of the Specimen was an ovoid, well encapsulated growth measuring 6 x 4 x 4 cms. It was nodular on surface and was firm to feel. It showed on cut section greyish, gelatinous cartilaginous areas interspersed with dense yellowish tissue (Fig 10).

Microscopical examination The sections showed a typical structure of an intracanalicular fibro-adenoma. Section through dense glistening cartilaginous areas (as seen on naked eye inspection) showed scattered areas of cartilaginous tissue (Fig 11). There was no evidence of proliferative activity either of the epithelial cells or of the stroma cells suggestive of a malignant transformation.

This presents a very interesting example of a fibro-adenoma undergoing transformation of the stroma. It is interesting to compare these changes with those occurring in the breasts of dogs where the bone formation is not an uncommon occurrence. Irregular shaped cartilage can be seen in many parts of the tumour and

surrounding the glandular elements that exist in these parts. At some places the cartilaginous portions begin to calcify. All changes in these neoplasms point to a transformation of fibrous tissue elements into cartilage, and such cartilaginous changes in human breast are extremely rare.

SUMMARY

1 Five cases of mammary gland fibro-adenoma showing unusual features are presented.

2 Two of these show changes occurring during gestation and lactation. The microscopical changes brought about as a result of gestation and lactation in a pre-existing fibro-adenoma may lead to difficulties in diagnosis and as a result the patient may be subjected to an unnecessary major operation.

3 Two cases of malignant changes occurring in a fibro-adenoma are presented. One of these is of the nature of a sarcoma and another a carcinoma.

4 The cartilaginous changes occurring in fibro-adenoma in human breast is extremely rare. One such case is reported in this paper.

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THE MARROWGRAM IN HEALTHY INDIANS

AS STUDIED BY STERNAL PUNCTURE AND SMEAR PREPARATIONS

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The numerical and the morphological features of the peripheral blood are not always an accurate reflection of the activity of the haemopoietic system. Diseases of the haemopoietic system may occur without demonstrable changes in the blood picture, others may produce, during their course, extremely complex and puzzling alterations (Custer, 1933). The same changes may be brought about by many diverse pathological conditions (Dameshek, 1935). With our changed concept, the term 'blood diseases' has gradually given place to the more accurate term 'diseases of the blood-forming organs'. Of these, latter, the marrow, forms the largest component. In the adult, active marrow forms 35 to 6 per cent of the body-weight, in weight it equals the liver, and, in volume, (about 4,000 c cm) exceeds it (Whitby and Britton, 1946). Studies of the bone marrow, therefore, should furnish reliable indications of normal, or, disturbed haemopoiesis.

At the autopsy the marrow from any and all the bones is available for study by any of the methods. With reference to this Custer and Ahlfeidt (1932) Dameshek (1935) and Jaffe (1936) have reported their observations on the disposition of the marrow in normal persons. In the living patient, a button of marrow can be obtained by a trephine, and, imprint preparations, or, histological sections studied. Ghedini (1908) was the first to trephine and scrape the tibia and Peabody (1927) utilised this method for his classical studies of the marrow in pernicious anaemia. Donovan (1909) and Seyfarth (1922) preferred the flat bones like the rib, or, the sternum. Planese (1903) was the first to aspirate the marrow. Caronia (1922) practiced needle aspiration from the tibia in children, but, to Arinkin (1927) must be given the credit for reviving the method of Planese and popularising it as a simple and a safe procedure for marrow biopsy. The advantages and disadvantages of the various methods of obtaining marrow specimens, and the relative merits of sections, imprints, and smears for their detailed study have been discussed in detail by Osgood and Seaman (1944).

Custer and Ahlfeidt (1932) have shown that the marrow of the sternum remains active throughout life and is very sensitive to all forms of stimuli. Nordenson (1935) punctured several bones, normally containing red marrow, in the same patient, and, found that the marrow from each was similar both in quality and cellularity. In spite of the irregular distribution of cellular marrow in any bone, and, notwithstanding certain inherent weakness in its study by the technique of aspiration, sternal puncture has come to stay as the method of choice in marrow examinations.

Many have studied the composition of marrow in normal healthy persons (Young and Osgood, (1935), Segardhal, (1935), Vogel, Erf and Rosenthal (1937), Bodley Scott (1939), Pitts and Packham, (1939) etc) For our country the only figures available are those of Napier and Sen Gupta (1938) and Napier and Das Gupta (1945) Osgood and Seaman (1944) compiled all the available data, a critical analysis of this showed that the selection of the subjects was not always beyond reproach, and, among the different workers there was a lack of agreement over the technique of marrow aspiration and the subsequent handling of the material. Worse still, no uniform criteria of cell identification and nomenclature were employed. In our study of the normal marrowgram, we have followed, as far as possible, the recommendations put forth by Osgood and Seaman (1944) in their review.

MATERIAL

Selection of Subjects —

Only 10 subjects could be studied. All were males. They were all healthy adults with good general nutritional status and without any history of recent illness. A general physical examination was made in every case. At the time of the sternal puncture, five c cm of blood was collected from a vein in oxalated tubes (Wintrobe and Landsburg, 1935) and later studied in detail (Wintrobe, 1933). Table I gives additional information about the subjects, and Table IIa and Table IIb set forth the results of the peripheral blood examinations.

Table I: The Subjects

Serial No	Age	Community	Diet	Place of Residence	General Criteria of Health
1	23	Hindoo	Non vegetarian	Bombay 5 years	Medical student
2	22	"	Vegetarian	Bombay Permanent	" "
3	23	"	"	"	" "
4	24	"	Non Vegetarian	"	" "
5	23	Parsee	"	"	" "
6*	30	Hindoo	Vegetarian	"	Surgical patient. A Vaginal Hydrocoele case
7*	30	Mohomedan	Non vegetarian	"	"
8*	34	Hindoo	"	"	"
9*	28	Mohomedan	"	"	An Inguinal Hernia case
10*	44	Hindoo	Vegetarian	"	A Vaginal Hydrocoele case

* All examinations were carried out before the operation

The Method of Sternal Puncture —

The technique followed was that laid down by Young and Osgood (1935). Briefly stated, this consisted of infiltrating the region of the puncture and a small area round about, from the skin down to the periosteum, with two per cent novocain solution. The sternum was punctured at the level of the sterno-manubrial joint in the midline, we used a locally manufactured slightly-modified Salah needle. When the needle was felt to be in the marrow a syringe

Table II a The Peripheral Blood

Serial No	Hb in gms	R B Cs in Millions per o mm	C I	V I	S I	M C V in u3	M C H in micro grams	M C H C	Reti- culocytes per cent	Icteric Index	B.S.R
1	16 0	5 1	1 08	1 08	1 08	85 6	31 4	34 5%	0 2	2 units	3
2	16 2	5 3½	1 04	1 03	1 0	83 6	30 0	32 4%	0 2	2 ,	1
3	14 5	4 8	1 04	1 08	0 07	85 5	30 2	35 3%	0 4	1 ,	2
4	14 5	4 85	1 08	1 00	0 95	81 6	20 0	32 6%	0 1	2	~
5	15 5	4 0	1 09	1 09	1 0	82 2	31 0	37 3%	0 0	2 ,	3
6	13 84	4 8	0 09	1 04	0 08	87 5	28 8	33 0%	0 4	1	3
7	14 8	5 2	0 98	1 1	0 08	90 2	28 6	30 0%	0 2	2	5
8	14 5	4 8	1 04	1 04	1 0	87 5	32 1	34 0%	0 4	0 5	6
9	15 0	5 2	1 1	1 1	1 03	82 3	30 0	32 5%	0 2	0 5 ,	3
10	14 5	5 1	0 08	1 0	0 98	84 3	28 4	33 0%	0 3	1	3

C I Colour Index (14.5 gms 100%)

V I Volume Index (C V 42 100%)

S I Saturation Index

M V C Mean Corpuscular Volume

M C H Mean Corpuscular Haemoglobin

M C H C Mean Corpuscular Haemoglobin Concentration

B.S.R (Wintrobe's method) Results of the readings of the end of 60 minutes

Table II b The Peripheral Blood (Contd)

Serial No	Total Leucocytes per c mm	Differential Counts %						
		Neutrophils			Eosinophils	Basophils	Monocytes	Lymphocytes
		Segmented	Stab	Juvenile				
1	7 800	60 0	1 0	0 0	1 0	0 0	2 0	36 0
2	9 000	57 5	7 0	0 5	2 0	0 0	2 0	31 0
3	8 500	40 0	1 0	0 0	3 0	0 0	1 0	35 0
4	8 600	41 5	1 0	0 0	4 0	1 0	1 0	51 5
5	8 400	40 5	2 5	0 0	6 0	1 0	3 0	41 0
6	5 500	48 0	2	0 0	2 0	0 0	3 0	43 0
7	~7,700	50	3	0 0	7 0	0 0	2 0	33 0
8	5 800	60	3	0 0	4 0	1 0	3 0	20 0
9	9 400	62	3	0 0	3 0	0 0	4 0	28 0
10	8 100	50	3	0 0	6 0	1 0	2 0	39 0

was attached to it and as nearly as possible one ccm of the marrow aspirated (Osgood and Seaman, 1944)

Further Manipulations with the Marrow-material —

The aspirated marrow was immediately transferred to a small oxalated tube containing 0.8 mgm of potassium oxalate and 1.2 mgm of ammonium oxalate and thoroughly mixed (Wintrobe and Landsburg, 1935). This material was utilised for all the subse-

investigations a differential count of the nucleated cells, peroxidase and reticulocyte counts, total nucleated cell counts were not done. For the differential count thin smears were prepared on glass slides from the oxalated specimens and stained with Wright's stain using a buffer phosphate solution with a pH of 6.4 for dilution. In every case one thousand nucleated cells were differentiated, two hundred and fifty cells being counted from four corners of the smear. The disintegrated cells were not accounted for. The peroxidase stains were prepared by the method of Osgood (1940), five hundred cells were classed. For the reticulocyte counts one thousand red cells were scrutinised (Osgood and Wilhelm, 1934).

Nomenclature and Criteria of Cell Identification —

Not a little confusion exists in haematologic literature because of the use by different authors of so many different names for the same cell or, worse still, because of so many different cells having been called by the same name. Osgood and Seaman's (1944) suggestion for the preparation of an "Approved Standard Nomenclature for Haematology" is therefore most commendable. In our work the criteria for the identification of different cells and the nomenclature are those described by Israels (1939) and Whitby and Britton (1946). According to this, as far as the red blood cell series is concerned, (and over which most of the controversy exists) the most distinctive feature of any cell is its nuclear configuration, also the term erythroblast is applied to any nucleated red blood cell and the cell called megaloblast (defined precisely) does not exist in the normal marrow.

RESULTS

The results of our ten cases are expressed in Table III on page 35.

COMMENT

We believe we have satisfied all the criteria enunciated by Osgood and Seaman (1944) as regards the selection of subjects, adoption of a standard procedure, the collection of the material and its further manipulation, etc. These authors (1944), from the accumulated data of several workers, have calculated the tentative recommended standards for normal persons. Strictly speaking, these are standards for the people in the West. Napier and Sen Gupta (1938) have published the results of two series of cases. In their first series, (Napier and Sen Gupta, 1938) the marrow (2 cm) obtained by sternal puncture was studied in ten normal 'volunteers', however no details about these subjects of their study are mentioned. Their second series (Napier and Das Gupta, 1945) consisted of 53 persons, infested with filariasis but otherwise apparently healthy. There is obvious objection in calling such patients normal healthy individuals.

The total nucleated cells were counted in our first three cases. The figures showed such wide variations that we dropped the procedure in the subsequent studies. Napier and Sen Gupta (1938) had a similar experience but still believe, from their experience, that in diseased conditions there exists a co-relationship between

haemopoietic activity and the total nucleated cell count Zanaty (1937) sought the total nucleated cell count to be of little value and Bodley Scott (1939) calculated that statistical analysis did not confirm the significance of a numerical count. Our figure for the reticulocyte counts compare favourably with those of Napier and Sen Gupta (1938). The differential count is the most significant feature of the marrowgram. It reflects both the degree of cellularity (Zanaty, 1937) and what is more the quality of the most important constituent of the haemopoietic system.

Table IV The Comparison with Available Figures

Alternative Terminology		Osgood & Seaman (1944) (compiled) Tentative Recommended Standards	Napier & Sen Gupta (1938)	Bhende (1946)	Alternative Terminology
Granuloblast	Myeloblasts	0.40	1.20	0.10	
Pro granulocytes A&S	Premyelocytes	2.40	0.70	0.80	
Granulocytes	Myelocytes	3.20	5.70	6.42	
Metagranulocytes	Neutrophils Juvenile	6.50	0.70	5.83	
Rhabdocytes	Neutrophils Stab	24.00	25.30	14.00	
Lobocytes	Neutrophils Segmented	15.00	16.80	16.07	
	Eosinophiles	2.00	4.70	2.50	
	Basophiles	0.20	0.20	0.10	
	Monocytes	2.00	3.00	0.70	
	Lymphocytes	14.00	6.25	30.89	
	Hemocyto blasts			0.00	
Karyoblasts	Megaloblasts	0.20	0.70	0.00	Megaloblasts
	Proerythroblasts			1.07	
Prokaryocytes } Karyocytes } Metakaryocytes }	Normoblasts	11.00	3.40 21.60	18.75 0.00	Erythroblasts Normoblasts " Type I
				1.72	" Type II
				18.75	" Type III
	Disintegrated Cells	19.00	Not counted	Not counted	

Table IV gives a comparison of our figures with those of Napier and Sen Gupta (1938) and those calculated by Osgood and Seaman (1944) as the tentative normal standards.

SUMMARY

The Marrowgram as revealed by the sternal puncture smear preparation is studied in 10 healthy Indians.

I am most grateful to Dr N. D. Patel. He actually did the sternal punctures and secured the material in the first five cases. I also thank Drs V. P. Mehta and K. S. Shah for their help in obtaining the material for the study of the last five cases.

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BANTI'S SYNDROME

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The terms Splenic Anaemia and Banti's Disease which have unfortunately crept into literature and text books have been often times repudiated by various authors. The term Splenic anaemia was first introduced by Greisenger in 1866 to describe cases of splenomegaly with hypo-chronic anaemia. Since, evidence has been forthcoming that all chronic splenomegalies from whatever cause are invariably associated with this type of anaemia, this term is no longer accepted. The term Banti's disease referring to a symptom complex dominated by chronic splenomegaly and certain anatomic histologic changes for which no definite cause has been found, cannot be regarded as a separate disease entity. Many such conditions corresponding to Banti's description have a definite etiological factor and hence quite rightly, the term Banti's disease is discarded and Banti's Syndrome used in its place.

In 1866 Greisenger and Gretzel first discussed cases of splenomegaly with anaemia under the term splenic anaemia.

In 1894 Giado Banti initiated a real study of this condition. He described its essential clinical and pathological features, however, its aetiology was still an unsolved problem. Banti attributed it to a "Splentoxin and not due to venous congestion. Osler regarded it as an intoxication of an unknown nature. Boyd (1931) attributed it to a toxic agent causing parenchymatous degeneration accompanied by fibrosis of the liver and spleen. McNee (1934) considered it to be a result of high portal blood pressure—the changes in the spleen preceding the onset of hepatic cirrhosis. Macmichael (1934) believed it to be a primary portal or hepatic disorder. Rousset (1940) brought forward ample evidence to show that Banti's syndrome may be explained on a mechanical basis, i.e., portal bed obstruction with an associated portal hypertension. He analysed 15 cases of Banti's syndrome and in 8 of these a definite extra-hepatic obstructive factor of the nature of thrombosis of the splenic or portal veins and cavernomatous transformation of the splenic vein was found at operation. The liver in all these 15 cases was normal as indicated by pre-operative liver function tests. Naked eye examination of the liver and histological section of a piece of liver removed during the operation. In four of these cases there was evidence of portal hypertension as indicated by high venous pressure in the splenic vein, three to four times the peripheral venous pressure, measured during the operation.

Ravenna (1940) explained that the splenic congestion was an "active one" depending on the lesion of the small splenic arteries. These vessels are incapable of contracting and controlling the inflow.

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of blood resulting in an inevitable rise of portal pressure and ultimate fibrosis of the liver and spleen

Greppi and Lenzi (quoted by Ravenna 1940) admit that the first lesion responsible for the splenic congestion might be an arteriolar one. Experimental attempts to produce "active splenic congestion" in dogs, by Henschen and Howald (1929) resulted in the development of splenomegaly in 2 dogs out of 3. The term "Congestive Splenomegaly" suggested by Larabee (1934) substantiates the views of Ravenna and further weight is added by Piney's statement (quoted by Ravenna 1940) "that there seems to be little doubt that Banti's disease is essentially a pathological state of the vascular system of the spleen"

The question of cardinal importance is whether the splenomegaly is primary or secondary to portal or hepatic changes. It has been noted that cases of splenic enlargement are found without any lesion of the liver or with diverse stages of typical cirrhosis. There was enough evidence to warrant the assumption that this splenomegaly is either autonomous or co-ordinated with, but not dependent on the hepatic lesion. The intimate relation between splenomegaly and cirrhosis of liver in which the splenic enlargement constitutes, apparently at least, the primary lesion, forms the modern idea of Banti's syndrome.

Clinically The disease occurs in the 2nd and 3rd decades with an equal sex distribution. Banti (1894, 1910) described the manifestation in 3 stages

(1) *Prec-ascitic stage* of splenomegaly, anaemia, leucopenia and its resulting symptoms lasting for 3-12 years

(2) *Intermediary stage* A transitional stage of enlargement of liver, gastro-intestinal disturbances such as anorexia, nausea, vomiting, diarrhoea or constipation, gastro-intestinal haemorrhages and jaundice lasting from 12-18 months. It would be of value to note the relationship between haematemesis and digestive periods as during digestion the spleen enlarges and gets congested.

(3) *Ascitic stage* Terminal stage of atrophy of the liver with ascites, cachexia, oedema and terminating in death within 6-12 months from hepatic insufficiency.

Banti contended that in the 3rd stage the disease is indistinguishable from advanced Laennec's type of cirrhosis.

Pathology *Microscopically* the spleen is enlarged, firm, with a thickened capsule. On section it appears very congested and increase in fibrous tissue is clearly seen. The splenic congestion may be inferred from—

- (1) pronounced decrease of splenic volume after injection of adrenaline or after haemorrhage
- (2) The frequency of transitory or permanent ascites
- (3) The occurrence of gastro-intestinal haemorrhages
- (4) Evidence of hypertension in splenic vein

Histopathology Banti described a fine fibrosis as the most characteristic feature. It is supposed to commence in relation to

central arteriole of the lymph follicle and to extend so as to involve the entire follicle. At the same time there is general thickening of the fine reticulum of the pulp. The trabeculae are thickened and there is an increase in the number of venous sinuses with distinct endothelial lining. Perilarterial haemorrhages are common and the connective tissue fibres become encrusted with iron, forming the well known "Siderotic" or "Gandy-Gamna" nodules. The splenic vein is usually greatly distended and there is evidence of large collateral channels connecting the spleen with the stomach and diaphragm. The liver shows various degrees of portal cirrhosis and dilated oesophageal varices are common. The bone marrow shows a hyperplastic reaction.

Blood picture The anaemia is of microcytic type with a low colour index and a leucopenia of about 3,000-4,000 per cmm affecting chiefly granulocytes with a relative lymphocytosis. The bleeding coagulation time, fragility of R.B.C.'s are normal but the platelet count is not uniform. Rosenthal (1925) differentiated Banti's disease into two groups depending on the platelet count. The thrombocytopenic group in which there is an initial low platelet count and a thrombocytaemic, in which the platelet count is normal or slightly subnormal. In the former the platelet count rises to normal levels after splenectomy whilst in the latter the count goes on rising steadily and in some cases may even reach up to a million or more. The value of this differentiation is important from the point of view of post-operative thrombotic complications which are common in the thrombocytaemic group. Boyce (1932) regards the platelet count as the most valuable examination for estimating the safety of splenectomy. Kelly (1929) considers that the platelet count should be below 200,000 before operation is undertaken.

Value of sternal marrow studies in Banti's syndrome has been very ably pointed out by Lemarzi et al (1943). After examining the smears of 21 cases of Banti's syndrome and having compared them with 10 normal cases, they came to the following conclusion, that though there are variations in the findings among the 21 cases of Banti's depending on the stage of the disease at which the sternal puncture was done, the findings as compared with the normal cases are sufficiently helpful to be adopted as a routine diagnostic procedure. The following are the figures:

	Normal	Banti's syndrome
1 Vol of nucleated cells	6.2-6.8%	15.5% (140%) N
2 Fat Volume	3.2%	5.9%
3 As Normal Erythroid myeloid Ratio	2.75-1	1.22-1
4 Myeloid dispersion count		
(a) Megaloblast		0.4%
(b) Premegaloblasts		0.9%
(c) Myelocytes		10.8%
(d) Metamyelocytes		81.5%
(e) Band forms		33.3%
(f) Polymorphs		25.1%
5 Erythroid Dispersion Count		
(a) Prenormoblasts		2.6%
(b) Basophilic normoblasts		18.2%
(c) Polychromatophilic normoblasts		79.3%
(d) Orthochromatic normoblasts		5.0%
Megakaryocytes	52/mm Sq	865/10 mm Sq

The prognosis depends on the stage of the disease and whether splenectomy is done early enough to check the progress of liver cirrhosis. Rousselot (1940) from an analysis of his cases observed that a marked variation in the clinical behaviour in some of his splenectomised patients manifested by repeated attacks of haematemesis whilst others did not have this complication. He explained this discrepancy as follows

(1) The site of obstruction and (2) variations in the anatomical distribution of the veins forming the portal system may be the determining factors

Treatment It has long been known that the spleen is not an organ necessary for life, in fact, the ancients, on the erroneous supposition that the speedy giraffe did not possess a spleen, are said to have excised the spleens of runners in order to increase their efficiency. In view of this encouragement the surgeons need not counsel patience.

There exists at present a difference of opinion as to the ideal method of treatment for this condition. Some recommend conservative treatment whilst others, like our ancients, regard splenectomy as the ideal form of treatment. Still others, a little more cautious, prefer to choose their cases for a particular line of treatment. The grouping of cases into the thrombocytopaenic and thrombocytaemic as advocated by Rosenthal (*loc cit*) has been used by some authors as the index of selecting cases for splenectomy.

On the conservative side, Davidson (1934) advises large doses of iron to combat anaemia and chronic ill-health. Deep X-ray irradiation have been advocated to reduce the size of the spleen. This method has its disadvantages in that it leads to extensive adhesion formations causing great deal of discomfort and pain to the patient due to perisplenitis. Besides subsequent splenectomy, if desired may be extremely difficult to perform.

Ligation of splenic artery has been advised when for some reason or other splenectomy is difficult. Quite contrary to expectations the spleen does not become gangrenous but reduces in size and atrophies and eventually becomes fibrotic. Benhamon (quoted by Palit 1935) definitely condemns it. He says that necrosis is sure to follow. The procedure though suggested is rarely practiced.

Howells (1938) has reviewed 43 cases treated medically with a mortality of about 49 per cent. 20 cases or 46 per cent improved under this regime and 2 cases did not show any improvement.

TABLE I

No. of cases	Stage of Disease	% Improvement
10 out of 10	1st	03%
" out of 18	2nd	30%
3 out of 9	3rd	33%

From the above table it is noted that the best results are obtained in the last stage of the disease according to Banti's classification.

The advocates of splenectomy have advanced the following arguments to support their contention

(1) The removal of large abdominal tumour causing chronic ill-health and in validism

(2) Relief of portal congestion and lessening the risk of haemetemesis

(3) Removal of an unhealthy spleen which may act as a store house for toxins

(4) Guarding against the possibility of rupture

(5) In the presence of ascites the splenectomy may be profitably combined with some form of Talma-Morison operation

Palit (1935) performed 33 splenectomies for cases of chronic malaria and Banti's syndrome with only 2 deaths or 6 per cent operative mortality

Bar and Bulin (1940) performed 22 splenectomies with 6 deaths or 27 per cent operative mortality 3 of these patients died as a result of continued bleeding from the sites of adhesions They reported very favourable influence of splenectomy on ascites Of the 6 patients on whom paracentesis was performed before the operation only one of them continued to have reaccumulation of fluid after the operation In cases with ascites they advise rotation and fixing the greater omentum in the splenic bed to increase the collateral circulation rather than doing a Talma-Morison's operation

Howells has given some interesting figures of 51 splenectomised cases 9 patients died soon after the operation or 18 per cent operative mortality Of the remaining 42 patients 17 died of complications over a varying period 3 patients did not show any improvement and the remaining 22 cases were improved or 43 per cent improvement

TABLE II

No of cases	Stage of Disease	% Improvement.
14 out of 25	1st	56%
3 out of 10	2nd	30%
5 out of 16	3rd	31%

Here again the figures indicate the best results from operative treatment are obtained in the initial stages of the disease

From his review of 94 cases treated both medically and surgically Howells (1938) considered that splenectomy did not improve the expectation of life nor influence the recurrence or progress of cirrhosis, anaemia or haemetemesis Rousselot (1940) reported that 9 of his patients had recurrent intestinal haemorrhages following splenectomy and only 6 were relieved Fox (1933) in a series of 14 splenectomies found that 6 out of the 8 patients who were followed up from 3-8 years continued to have haemetemesis This variation in the clinical behaviour of some patients has already been explained

In all, 7 cases labelled as Banti's syndrome have been treated surgically in the KEM Hospital during the last 20 years 5 of the 7 excised spleens on histological section showed changes resembling those described for Banti's spleen The remaining 2 did not show all the changes of the Banti's type but they do show some increase in the fibrous tissue, dilatation and congestion of sinusoids, periarterial haemorrhages and sideotic nodules but the fibro-andemic were missing In view of the close clinical and pathological similarity the author has taken the liberty to include these 2 cases in the present discussion An analysis of the cases is presented herewith

Age and Sex Average age of these seven cases is 20 years, youngest patient was 15 years old and oldest patient was 45 years There were five males and two females The discrepancy is due to greater number of males attending this hospital There were six Hindus and one Mohamedan

Clinical Manifestations Distensions of abdomen, generalised weakness and an enlarged spleen were the constant features of every case All of them gave a history of irregular intermittent fever of some duration before the symptoms were noticed This made a differentiation from chronic malaria difficult Repeated negative blood smears and an absence of response to quinine therapy were the features on which reliance was placed Ascites was found in 3 cases and an enlarged liver in 3 cases Subjective gastrointestinal symptoms were present in all cases and haemetemesis in only 2 cases There was no malaena Jaundice in one case and engorgement of veins and oedema of feet in 2 cases

Blood picture Microcytic anaemia and leucopenia was present in every case and the platelet count in 4 cases was of the thrombocytopenic type and in 2 of the thrombocytaemic type In one case the count is not recorded The bleeding and conglutination time and fragility of R.B.C's were normal

Treatment

Pre-operative Large doses of iron and blood transfusions were given

Operative Treatment Splenectomy was performed in all seven cases 6 survived the operation and one died after the operation due to repeated attacks of haemetemesis Of the remaining 6, 2 died subsequently—one on the 8th day after operation as a result of hepatic failure and the other on the 27th day due to staphylococcal meningitis The operative mortality was about 14 per cent

Table III

Case No	Stage of disease according to Banti's class	Incision	Type of operation	Operative findings		
				Free fluid	Splenic adhesion	Liver
1	1st		Splenectomy	other findings not available		
2	3rd	Left Paramedian Transverse	Splenectomy			
3	3rd					early cirrhosis
4	3rd	Left Paramedian	Splenectomy			Hobnail type
5	3rd	Left paramedian Transverse	Talma Morrison			
6	1st		Splenectomy			
7	2nd	Left Paramedian				
Stage I — 2 cases		Stage II — 4 cases		Stage III — 4 cases.		

The case number seven of stage 2 died of haemetemesis within a few hours of operation

Post operative complications 3 patients developed left sided basal congestion and consolidation but improved with treatment One patient developed jaundice on the fourth day after the operation and subsequently died of hepatic failure One developed haemetemesis and died soon after the operation

Discussion The etiology of Banti's syndrome is still an unsolved problem though the consensus of opinion favours the vascular changes in the spleen In our series of cases thorough examinations of the portal venous bed have not been made to detect any extra-hepatic obstructive factors

The diagnosis from other chronic splenomegalies is usually made by exclusion The guiding features are splenomegaly, microcytic anaemia and leucopenia Liver function tests carried out as a routine will usually rule out any hepatic diseases and will also serve as a useful guide for treatment The value of sternal marrow studies as an aid to diagnosis has still to be proved with a wider use on a large series of cases Some interesting haematological information will be forthcoming

The usefulness of splenectomy as a, justifiable procedure has been well established Moreover, Howell's figures leave very little choice It is an unanimous opinion that by far the best results with splenectomy are obtained when performed in the early stage of the disease, hence the need for an early diagnosis Four of our patients were in the third stage when splenectomy was carried out One in the second stage and two in the first stage In spite this our immediate operative results have been satisfactory

Splenectomy, however, does not check the progress of the liver disease, although its favourable influence on ascites has been noted The most feared complication after splenectomy is haemetemesis As a safeguard against it, the ligature of the left gastric vein has been advised It should be further impressed that a thorough examination of the portal venous bed must be carried out during operation to detect any extra-hepatic obstructive factors and also a piece of liver be excised for a histological examination should there be any suspicion of liver disease

It is only when our cases are systematically studied and recorded that we hope to contribute our share to the advance in medicine

SUMMARY

- (1) A survey of the aetiological, clinical, pathological manifestations and diagnostic procedures, is given
- (2) The value of conservative treatment and splenectomy for Banti's syndrome is assessed
- (3) An analysis of seven cases treated in the K.E.M. Hospital is given

(My thanks are due to the Dean, K.E.M. Hospital and the members of the Honorary staff for allowing me to report their cases and to Dr J. C. Patel for help and encouragement)

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Discussion

Dr A Hameed considered that splenectomies should not be carried out unless the spleen was large and caused discomfort. The operation should not be done if cirrhosis of the liver was present. He discouraged removal of the spleen in all cases of splenic anaemia unless it was determined that the spleen was the seat of the disease. He considered the operation dangerous as it was followed in 50 per cent of cases by a fatal haematemesis, due to thrombosis of the veins.

Dr M J Shah enquired whether the four cases which had survived were followed up especially to detect the development of cirrhotic changes in the liver. From Howells' figures (loc cit) it was evident that no case had been made out for surgical treatment.

Dr R G Chitre enquired whether liver function tests were carried out before or after splenectomy in these cases.

Dr S G Joshi enquired the criteria used for the diagnosis of Banti's disease and its medical treatment.

Dr A V Baliga said that while there was no specific medical treatment surgery offered some hope. He cited two cases, where he had carried out the operation successfully, both the patients being alive twelve years later. He added that one of these patients disregarding his advice visited a place of high altitude where he developed haematemesis.

Dr J C Patel said that in the light of recent experimental and clinical work it was common knowledge that the cause of the cirrhotic process in the liver was a deficiency of unknown origin in which the sulphur containing amino acids and choline, a member of the B complex group of vitamins were supposed to be involved. In his opinion cirrhotic changes in the liver in cases of splenic anaemia may be prevented by the administration of a high protein diet and large doses of Vitamin B complex. He referred to the recent papers published in the American Journals where with this treatment in cases of cirrhosis of liver with ascites responded favourably.

Dr R G Chitre said that in addition to nutritional deficiency, other factors probably existed in the causation of the disease.

Dr P K Sen speaking in favour of splenectomy said that removal of the spleen would considerably reduce the congestion in the portal tract. He added that at the same time, Talma-Morrison operation could be carried out in cases where it was indicated.

Dr O V Jooma replying agreed with Dr Hameed that haematemeses was a serious complication after splenectomy and could be obviated by ligaturing the left gastric vein. Replying to Dr Shah he said that the only case that was followed was for six months. He agreed with Dr Chitre that liver function tests were useful.

Dr R G Dhayagude at the outset emphasised the fact that Banti's was not a disease but a clinical syndrome based on the observations of Banti that in a certain number of cases a progressively enlarged spleen, secondary (microcytic) anaemia, characterised by an insidious onset, haematemeses and cirrhosis of the liver in children or adults below the middle life were found to be associated. The pathological changes in the spleen which was the most significant findings in the post-mortem room were worked out later and the description of changes in the early stages of the disease—the so called fibro-adenic—was quite characteristic. If the spleen showed these changes and also contained siderotic—Gandy-Gamna nodules—the diagnosis from the appearance of the spleen was not difficult. But if the spleen had undergone changes a stage farther than those mentioned above fibrosis only was visible. It is in such cases that a pathologist may be helpless in stamping a particular spleen as being definitely of Banti's disease.

The diagnosis of Banti's disease is a diagnosis by exclusion and therefore Banti's is not even a clinical entity, as there are no definite clinical criteria to clinch the diagnosis. In this state of ignorance since the removal of spleen is attended with a certain amount of mortality, it seemed to him a non-clinical person that medical treatment should obviously be a course of choice in early cases. If haematemeses had once taken place since there was a chance of a severe recurrence against splenectomy appeared to be justified. As a matter of fact in all ill-understood conditions like Banti's it is only a close co-operation between the physician, surgeon and the pathologist that will help in a better understanding of the diagnosis and treatment of these cases.

Critical Notes and Abstracts

BENADRYL AND PYRIBENZAMINE IN ALLERGIC CONDITIONS—Epstein S (Wisc med journal, May, 45 489-496) reports that management of the allergic patient remains rather unsatisfactory in spite of the good results obtained in many instances by proper allergic management and symptomatic control. In recent years antihistaminic drugs have been introduced that afford control of the symptoms in some allergic conditions, notably urticaria, hay fever, asthma, and allergic dermatitis.

The use of antihistaminic substances in allergic conditions is based on the assumption that histamine plays a role in their causation. Somewhat simplified, the theory may be presented as follows, using as an example an individual who has become allergic to ragweed pollen and presents the symptoms of hay fever. The ragweed is called the allergen or antigen. The individual becomes sensitized to the antigen (ragweed). The sensitized individual produces specific antibodies to this antigen (ragweed), fixed antibodies settle in the mucous membranes of the nose and conjunctiva, and determine the localization of the clinical symptoms, in this instance, hay fever. Upon renewed exposure to the antigen (ragweed pollen) an antigen-antibody reaction occurs at the shock organ. The antigen-antibody reaction leads to release of histamine or a histamine-like substance. This substance causes inflammation of the cells of the shock organs (conjunctiva, and nasal mucosa), and thus produces the clinical symptoms of hay fever.

In 1937 and 1939 Bovet and Staub at the Pasteur Institute in Paris detected the anti-histaminic activity of certain derivatives of amino-ethanol and ethylenediamine. In USA, Parke, Davis and Company developed "Benadryl" and Ciba Pharmaceutical Products, introduced "Pyribenzamine," both crystalline white powders soluble in water, and both having remarkable similarity in regard to their physiologic and antiallergic action, so that one may discuss them both together. Both have a very low toxicity when given orally, but appear rather toxic when injected intravenously. They are both highly specific against histamine, but are also mildly effective against acetyl choline and probably possess additional pharmacological properties as evidenced by their sedative effect. Therefore the fact that allergic condition is relieved by pyribenzamine or benadryl is not absolute proof that the condition was caused by the release of histamine.

Urticaria Acute urticaria and urticarial drug eruptions respond to pyribenzamine and benadryl better than any other allergic condition (about 95% improved in acute urticaria and 80% in chronic). The itching is usually relieved first, then the swelling and hives disappear, at times extremely rapidly. In acute cases that normally last only a few days, this amounts to practically a cure. In chronic urticaria most cases derive symptomatic improvement, as a rule, the urticaria recurs when the drug is withdrawn and is again

brought under control when medication is resumed. In some cases the effect of the drug seems to wear off under these circumstances.

Hay Fever and Allergic Rhinitis These conditions respond very well to benadryl and pyribenzamine (80% improvement in hay fever and extrinsic allergic rhinitis). Apparently the pollen sensitive cases are benefited most, the effect is not so good in extrinsic allergic rhinitis, that is in cases with allergy to dust and foods. The results are still poorer in the so called intrinsic rhinitis where external allergens cannot be demonstrated.

Asthma The results in bronchial asthma so far are somewhat disappointing (about 40-50% improvement).

Atopic Dermatitis The evaluation of the antihistaminic drugs in atopic dermatitis (allergic eczema) is very difficult. There has been relief of pruritus, but no objective changes in longstanding atopic dermatitis, although acute exacerbations have been definitely checked in some cases. The results have been encouraging in pruritus vulvae and anal pruritus and disappointing in contact dermatitis and infectious eczema. It seems also of value in erythema multiforme. The few available reports in regard to migraine, and Meniere's disease are disappointing, but occasionally a case has been helped. Antihistaminic drugs also have been useful in preventing allergic reactions from medications. Pyribenzamine given simultaneously with insulin has suppressed urticaria in a patient who reacted thus to all forms of insulin.

Dosage and Administration The dosage for both drugs is identical. Oral administration only is recommended at present, the average dose being 50 mg 3 or 4 times a day. If the symptoms are controlled the dose is reduced to one-half or less, if not, the dose may be doubled and 100 mg given 3 or 4 times daily.

Reported side effects have been chiefly sleepiness or drowsiness and dizziness. Less frequently dryness of the mouth, nausea, and diarrhoea have occurred.

VITAMIN—K IN URTICARIA McInnes, K. B. (South Med & Surg, 1946 108-109) states that one more drug has been added to the long list of those used in the treatment of urticaria, this being menandione, or synthetic vitamin K. Twenty milligrams are given in four divided doses the first day and fifteen milligrams the second and third days. The author employed this "short cut" almost routinely in all urticaria and angioneurotic edema cases immediately, then went ahead with the investigation. To date no unfavourable reactions to the drug have been encountered.

Clinical Case Reports

ACOUSTIC NEUROMA—N D Patel, MD (Lond), M.R.C.P (Lond)

J G a Christian aged 29, clerk in a business firm, was referred to me by an ophthalmic surgeon, whom he consulted for progressive diminution in vision. The history was that the patient started getting pain in the right ear some nine months ago. There was some pain in the right side of the head also. This was relieved by taking aspirin and he did not seek medical help. After a month or so weakness of the right side of the face appeared and he felt some difficulty in chewing. The pain in the head now spread to the right temporal region, inferior orbital margin and right cheek. He noticed some impairment of hearing and noises in the right ear. The hearing in the right ear progressively deteriorated, and the noises in the ear disappeared. There was no giddiness. He did not consult anybody for his "ear trouble". A month later his vision showed signs of impairment for which he consulted an oculist. Glasses and drops were prescribed which he went on using for three months. During this time the vision progressively deteriorated, headache became more general, and there was occasional vomiting. Sometimes he felt pain in the neck and some stiffness. There was no history of ataxia or fits. There was nothing of importance in the family history. He had suffered from malaria and typhoid fever some 12 years ago.

The physical examination showed some disturbance(?) of right olfactory nerve, loss of vision in both eyes, no perception of light, only movements recognised in the left temporal field, marked papilloedema both sides, no nystagmus, movements of the eye muscles normal, pupils dilated, central, circular, and equal, reaction to light very sluggish, to accommodation normal, some diminution of touch and pain sensation on the right cheek, right corneal reflex absent, facial paralysis of peripheral type on the right side, complete loss of hearing on right side, left ear hearing normal. Caloric test left ear giddiness started after 30 seconds, right ear, no giddiness, no response both right vestibular and cochlear nerves. IX, X, XI, and XII cranial nerves normal. Examination for motor functions showed hemiparesis on the right side with exaggerated right knee and ankle jerks, absent right abdominal reflexes and Babinski type planter response on the right side. There were no sensory changes, no inco-ordination or involuntary movements. The sphincters were not affected. Blood pressure 108/72 mm Hg. Heart, lungs and abdomen normal. Blood Kahn negative. X-Ray of the skull showed evidence of increased intra-cranial pressure. There was no erosion of the petrous ridge. No special plate taken to note any alteration in internal auditory meatus. A diagnosis of intracranial tumor in the posterior fossa was made, and the case referred to Dr R N Cooper for operation. On exploration on 15-10-1946 a tumor was seen in the right cerebellum-pontine angle, which appeared to be separate from the VIII nerve. It was removed in bits by special forceps. The pathologist's report on the specimen submitted was that it showed the characters of a neuroma.

The acoustic tumours are not uncommon in Bomba

cal picture is cleancut and diagnosis is not difficult. The results of surgical treatment are very gratifying if diagnosed and operated on early. As the welfare of the patient depends on the early diagnosis, familiarity with its life history is a necessity for every practitioner. The case presented here is rather atypical in many respects. A typical case of acoustic tumour presents what is commonly known as a syndrome of the cerebello-pontine angle. In this area some *twenty* different lesions have been described which may produce the syndrome. The commonest of these being acoustic neuroma, trigeminal neuroma, glioma of pons, meningioma, cholesteatoma (dermoid type of tumor), serious arachnoiditis, or a cerebral tumour breaking through the tentorium and blocking the angle. Dr. Y. M. Bhende of our Pathology Department has recorded *two* cases of *epidermoids* (cholesteatomas), one, an incidental discovery at the post-mortem in a Hindu youth of 21, who died of a tram-car accident and the other, in a Hindu youth of 25, who had excruciating pain over the left half of the face of six months' duration, and whose trigeminal ganglion was injected with alcohol without any relief. He died twelve hours after an operation for trigeminal ganglionectomy. A partial autopsy showed an epidermoid tumour in the left cerebellopontine angle, pressing on the trigeminal ganglion and the sensory root of the trigeminal nerve. The clinical picture produced by the different lesions of cerebellopontine angle is very characteristic. The following *chronological appearance* of symptoms and signs is to be greatly emphasised in making an early diagnosis—(1) Tinnitus, (2) nerve deafness, both irritative symptoms, disappearing when the nerve is destroyed, involvement of the vestibular portion of the VIII nerve,—dizziness or unsteadiness, but never systematized vertigo, and "absence of response to all canals from the nerve on the side of tumour, absence of response of the vertical canals from the nerve on the opposite side but presence of response from the horizontal canal from the nerve on the opposite side is known as the typical angle-picture" (3) occipital or suboccipital discomfort, stiffness or pain, (4) involvement of neighbouring cranial nerves, VII & V, facial weakness or spasm, absence of corneal reflex, diminished sensation on the face, and tic douloureux, (5) enlargement of the internal auditory meatus and erosion of the petrous ridge, (6) homolateral cerebellar symptoms, (7) signs of pressure on the pyramidal tract, (8) involvement of IX and X cranial nerves dysphagia, and guttural, slurring speech, (9) increased intracranial tension with affection of the optic nerves with choking of the discs, and rarely, (10) involvement of the olfactory nerve with loss of sense of smell, as a result of tremendous pressure over a long period of time, (11) involvement of III, IV and VI nerves, (12) cerebellar fits or decerebrate rigidity, and even (13) cerebrospinal rhinorrhoea.

The symptoms depend on the type, duration and situation of the tumour. Fibromas grow very slowly and take years to develop, sometimes as long as thirty years. Some tumours grow fairly rapidly. The usual history is of two years' duration. The neuroma or neurofibroma of the VIII nerve is a benign growth, encapsulated, and at least, theoretically curable.

Book Reviews and Notices

1946 YEAR BOOK OF GENERAL MEDICINE Edited by G F Dick (Infectious Diseases), J B Amberson (Chest), G R Minot and W B Castle (Blood forming organs and Kidney), W D Stroud (Heart and Blood Vessels) and G B Eusterman (Digestive System and Metabolism) Chicago The Year Book Publishers, Inc. 1946 Pp 772, Price Rs 15

The Year Book Publishers print a quiz of some 20 questions "just a sampling of the scores of positive new advances and new refinements in diagnosis and treatment" It is a good exercise for the reader to find out how many questions he can answer, and which ones he is prepared to accept as positive new advances! The plan of these year books is different from that of the Medical Annual There are 14 year books dealing with different branches of clinical medicine and surgery, in which articles appearing in medical journals all over the world are abstracted Hence it is inevitable that the articles should vary in their importance, some excellent, some good, while others indifferent, and a few hardly deserving the honour of reprint Though the editors give critical notes here and there, the reader has to use his critical faculty and remain vigilant lest the printed word hypnotises him in blind acceptance The volumes are more suited for the needs of the specialists than for general practitioners Bernoulli finds emetine to have a salutary effect on septic infections, accelerating the formation of agglutinins and spontaneous phagocytosis of leukocytes Its primary effect appears to be a general acceleration and positive catalysis of the defense mechanisms of the entire organism Bishopp gives a formula effective against human scabies and lice benzyl benzoate 68, ethyl p-aminobenzoate 12, sorbitan mono-oleate polyoxyalkylene ether derivative 14 and DDT 6 per cent This material diluted, 1 part to 5 parts of water, is applied to the entire body Butler and Reyersbach advise the use of 3 Gm of magnesium sulphate in 150 cc of 5 per cent glucose in water, injected intravenous in a 40 minute period, to overcome vasoconstriction in acute haemorrhagic nephritis If this does not reduce blood pressure, bilateral lumbosacral sympathectomy is advised Bridges, Wheeler and White suggest low sodium diet (700 mg Na), and free fluid intake in congestive heart failure By this regimen oedema which does not response to usual measures can be controlled and mercurial diuretics are needed less often, and frequently can be entirely eliminated 1500 cc to 1800 cc fluid may be allowed if the specific gravity of urine is 1010 or above, or if there is an intercurrent infection as much as 3000 cc of water may be allowed

INTERNATIONAL MEDICAL ABSTRACTS & REVIEWS, a monthly journal edited by Jyoti Dhar Calcutta Alipore P O No 5 pp 40 Annual subscription Rs 12

We welcome this new venture of Dr Dhar Medical journals of desirable standard and efficiency are few in India We hope this journal will maintain the high standard of the first number and will meet the needs of the general practitioners by supplying them abstracts of the articles which will be of use in their daily work

Reflections and Aphorisms

ON REFLEXES

"The reflex phenomena observed may be grouped under five heads (1) True muscle reflex (often dubbed as tendon, bone, periosteal, joint, fascial, aponeurotic &c), (2) Associated movements, (3) Spinal automatism, (4) Defence reflexes, and (5) Postural reflexes

Babinski's sign is a part of Marie-Folx manoeuvre for elicitation of the flexor withdrawal reflex Gonda's tendon stretch sign is a modification for eliciting the same reflex

Pronounced increased intracranial pressure brings about prompt diminution or abolition of the knee jerk However, a slight increase of intracranial pressure, such as that produced by prolonged jugular compression, coughing, pulling the hooked hands apart, or bending the trunk, will make the deep reflexes more apparent

When a deep muscle reflex is being elicited, a slight voluntary contraction of the muscles involved in this reflex must first take place The invisible reflex may then become visible and the weak one appear stronger

An excellent method to obtain reinforcement of the knee jerk is to have the subject, with knees slightly flexed, gently press the ball of his foot against the examiner's free hand

While eliciting the patellar reflex the patient pushes his leg slightly forward, the examiner opposes this movement with his left hand and simultaneously strikes the patellar tendon with the hammer held in the right hand For the Achilles reflex, the patient is asked to push the ball of his foot slightly downward so that the calf muscles are innervated, the examiner opposes this movement with his hand and so controls the pressure exerted by the patient The Achilles tendon is tapped the moment the patient presses his foot down

The essentials to obtain a muscle reflex are relaxation, with slight active flexion, that is increased innervation and tension of the muscle concerned, sudden, quick, sharp and brief stroke, diversion of the patient's attention, and some manoeuvre to increase slightly the intracranial tension

Superficial or skin reflexes are indirect or referred muscle reflexes, where a variety of stimuli of the distant reflexogenous zones will produce the contraction of the muscle They have extensive reflexogenous zones, their latent period is longer, and they are dependent entirely on the strength of the stimuli and on their summation, their fatigability is greater Whereas every muscle has its deep muscle reflex, only a few muscles have their superficial reflexes as well The essence of the stimulus in eliciting the superficial reflex lies in the quickness of the strokes and in the summation of the stimuli produced by long longitudinal or transverse brisk strokes "

WARTENBERG

Our Problems—a forum for discussion

SCIENCE IN INDIA

"Effectively science in India only began in the twentieth century. We can say with certainty that *there are latent in India great possibilities for scientific development*, the mathematics of Ramanujan and the physics of Bose and Raman have already shown that Indian scientists can reach the first ranks. Nevertheless, the difficulties under which Indian science suffers will preclude, as long as they last, any large-scale development, or, more particularly, any serious influence of science on Indian culture. It is inevitable that in science as in other aspects of life the Indians should feel the need for national self-assertion, but this attitude is always an uneasy one. *The Indian scientist must, in the first place, learn his science through English channels and be subjected to the patronising and insulting habits of the English to then subject races.* The reaction to this breeds a mixture of *submissiveness and arrogance* that between them inevitably affect the quality of the scientific work. Indian science is noted at the same time for the *originality* of many of its conceptions and experimental processes, and for extreme *unreliability* and *lack of critical faculty* in carrying out the work itself.

Needless to say, Indian science, like everything in India except the English Civil Service and the Army, is starved of funds. The total annual sum available for scientific research in India is probably not more than £250,000, which would be equivalent to 1/50 of a penny per head of population, or 0.15 per cent of the miserable national income of £1,700,000,000. Yet there is hardly any country in the world that needs the application of science more than India. In order to release the enormous potentialities for scientific development in the Indian people, *it would be necessary to transform them into a self-reliant and free community. Probably the best workers for Indian science today are not the scientists but the political agitators who are struggling towards this end."*

J. D. BERNAL, F.R.S.

MEDICINE IN INDIA

"Let us consider the present state of modern medicine in India. It was introduced into India with the advent of the British rule and it has steadily developed into the state-accepted system of medicine in this country. Its progress has been very slow. Until a few years back we could not boast of any well organised medical profession. As regards its practice it still remains confined to big towns and Rural India is unprovided with qualified and scientific medical relief. Modern medicine is said to be foreign and is looked upon with prejudice, not only by the illiterate masses but also by the intelligensia. They do not know that this system of medicine is no more western than eastern. It is only by a sheer historical accident that its message has reached us through the British. It is absolutely certain that, even otherwise, modern medicine would have reached us all the same. Modern medicine is universal and

its appeal is to the entire world. It is a science and science knows no distinction of caste, creed or colour. It welcomes knowledge from whatever quarter it comes. It has no prejudice against any particular system or source of knowledge. It is the outcome of the sum total of the entire world's contribution to the existing knowledge and such contributions have not been the privilege or the property of any one nation. Its scope is being enlarged constantly, consequent on the work of its votaries who are spread all over the world. Every civilised country has made and is making an effort to grasp each new advance and use it for the welfare of its people. Japan has got the inspiration from Dutch, and Turkey through French and later German sources. China and Afghanistan have also adopted modern scientific medicine. There is not one country in the world which denies itself the benefits of the modern scientific medicine. It is therefore unfortunate that we should find still in India a certain prejudice against the modern scientific medicine arising out of false sense of national pride and prestige. *People do not talk of a western physics and an eastern physics or of a western chemistry and an eastern chemistry.* Sir P C Ray, the great Indian scientist, who established and proclaimed to the world the greatness of ancient Indian contribution to chemistry, never advised his countrymen to rest content with its blissful contemplation, on the other hand he spared no pains or effort to the encouragement and advancement of study of modern chemistry in India. It is difficult to understand why with regard to medicine alone that people should persist in talking of eastern and western systems of medicine."

B T RAO FRCS (Ed)

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Original Contributions

QUINIDINE IN THE TREATMENT OF AURICULAR FIBRILLATION

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Senac (1749) observed that "rebellious palpitation" of the heart could be controlled by quinine (White). Evidently it must be cinchona bark because quinine was isolated by Pelletier and Caventon only in 1820. Quinidine was prepared and named by Pasteur (1853), although it was described earlier by Van Heyningen (1848). Oppolzer (1866) used quinine in addition to rest and digitalis in the treatment of heart disease. Wenckebach (1914) was told in 1912 by one of his patients, a Dutch merchant, that he could control his cardiac irregularity (auricular fibrillation) by taking quinine. Since Wenckebach did not believe him, the patient said that he will return next day with a regular pulse, and this he did after taking 15 gr of quinine. Frey (1918) found quinidine more effective in controlling auricular fibrillation. Since then successful results (7 to 94 per cent) have been observed by various authors, Levy (1922), Viko et al (1923), Korns (1923), Carr (1924), Elsmayer (1927), Bramwell and Ellis (1928), Wolff and White (1929), Morawitz and Hochrein (1929), Parkinson and Campbell (1929), Weisman (1932), White (1944), Levine (1945) and others.

The present paper deals with 7 cases of auricular fibrillation observed by the senior author and treated by quinidine. They consist of —

(1) Four cases of rheumatic heart disease,—2 involving the mitral valve alone (mitral stenosis), and 2 involving the mitral and aortic valves (mitral stenosis with aortic stenosis and regurgitation)

(2) One case of pulmonary hypertension with myocarditis and heart failure

(3) Two cases of thyrotoxicosis with exophthalmic goitre. Brief notes of these 7 cases are given below —

1 Rheumatic Heart

(a) Mitral stenosis

Case (1) K B, female aged 25 years, was admitted on 22-7-46 with a history of dyspnoea and palpitation of 4 months' duration. She was

married and has 2 children, both in good health, 1st 9 and the 2nd 4 years. As far as she could remember there was no history of fever or pain in the joints indicating rheumatic infection.

Physical examination showed a moderately nourished individual with dyspnoea, cyanosis, prominent jugular veins and oedema of the legs. Heart was enlarged, left border 2 inches outside the mid-clavicular line, right border right lateral sternal line. A systolic murmur was heard in the mitral area. Heart was irregular and showed auricular fibrillation. Blood pressure 130/80. Liver was enlarged 4 fingers below the costal margin. Lungs showed moist sounds at both bases. Urine was normal. Radiological examination on 29/7 showed enlargement of heart both towards the right and left, straightening of the left border and prominent pulmonary conus. Enlarged left auricle could be visualised both in the antero-posterior and in the right anterior oblique view with barium in the oesophagus. Right transverse diameter of the heart 1.5 inches, left transverse diameter 4.2 inches, total transverse diameter 5.7 inches, transverse diameter of the thorax 9 inches.

The patient was put on digitals and diuretics by mouth and mersalyl injections. Signs of congestive heart failure disappeared but auricular fibrillation persisted. Electrocardiogram on 27/8 showed auricular fibrillation and right axis deviation (Fig 1).

On 27/8 digitals were stopped and quinidine was started on the next day with a test dose of 3 gr. Second day she had 15 gr, 3rd day it was increased to 25 gr, and on the 4th day i.e., on 31/8 auricular fibrillation disappeared. 38 gr of quinidine controlled the auricular fibrillation. After its disappearance, a definite presystolic murmur could be made out in the mitral area. This dose of 25 gr of quinidine was continued for another 2 days more and from 3/9 it was reduced to 5 gr a day. The patient had 158 gr of quinidine in the course of 8 days and it was stopped. She gradually improved. On 14/10 electrocardiogram (fig 2) showed a regular sinus rhythm with right axis deviation. A second X-ray on 14/10 showed considerable reduction in the size of the heart, but the left auricle was still visualised in the antero-posterior view. Right transverse diameter of the heart 1.45 inches, left transverse diameter 3.7 inches, total transverse diameter 5.15 inches, transverse diameter of the thorax 9.8 inches. On 23/10 auricular fibrillation reappeared. The patient was put on 5 gr of quinidine every hour for 3 doses. The next day the auricular fibrillation disappeared. A maintenance dose of 5 gr was continued till 4/11, and the patient was discharged on 11-11-46.

Case (2) P. A., female aged 45 years, was admitted on 2-9-46 with a history of palpitation and breathlessness on exertion of one month's duration. She had 5 children one of them died at the age of 15 after delivery and another one is the previous case (No 1) of rheumatic heart with auricular fibrillation. There was no history of fever or pain in the joints indicating rheumatic infection.

Physical examination showed a fairly nourished individual with cyanosis, prominent jugular veins and enlarged liver. There was no

oedema anywhere Heart was enlarged, left border 1 inch external to the mid-clavicular line, right border $\frac{1}{2}$ inch external to the lateral sternal line Mitral area showed systolic murmur Heart was Irregular and showed auricular fibrillation Blood pressure 130/90 Lungs showed a few moist sounds at both the bases

The patient was put on digitals and diuretics by mouth and mersalyl injections Congestive heart failure symptoms disappeared but auricular fibrillation persisted Electrocardiogram (fig 3) on 11/10 showed auricular fibrillation, there was no right axis deviation On 13/10 the patient was given a test dose of 3 gr of quinidine On the 14th and 15th she had 15 gr a day On the 16th after the first dose of 5 gr of quinidine, auricular fibrillation disappeared 18 gr of quinidine controlled the auricular fibrillation Electrocardiogram (fig 4) on 15/10 showed normal rhythm, but sinus arrhythmia was present in addition Radiological examination on 16/10 showed enlargement of the heart both towards the right and left, prominent pulmonary conus and left auricular enlargement in the right anterior oblique view with barium in the oesophagus Right transverse diameter of the heart 19 inches, left transverse diameter 3.5 inches, total transverse diameter 5.4 inches, total diameter of the thorax 9.2 inches A maintenance dose of quinidine was then continued up to the 26th, and then stopped On the 30th, auricular fibrillation reappeared and was confirmed by electrocardiogram The patient was put on 5 gr of quinidine and normal rhythm was restored the next day A maintenance dose of quinidine was continued up to 4/11 The patient was discharged on 11-11-46 with considerable improvement and normal rhythm

(b) *Mitral stenosis with aortic stenosis and regurgitation*

Case (3) M P S, male, aged 26 years, was admitted on 23-8-46 with a history of breathlessness, palpitation and puffiness of the face of one year's duration He was married, had 2 children, the 2nd died at the age of 3 When he was a boy of 15 he used to suffer from occasional sore throat, low fever and polyarthritis and the condition was diagnosed as rheumatic at that time The present complaint started one year ago with palpitation on slight exertion The breathlessness gradually increased and for the past 2 months the condition has been worse

Physical examination revealed a moderately nourished individual with slight cyanosis, no oedema, no clubbing of the fingers Heart was enlarged, apex beat was in the 6th intercostal space 2 inches external to the left mid-clavicular line, right border just external to the right lateral sternal line A well defined systolic thrill was felt in the aortic area, systolic and diastolic murmurs were heard in the mitral and a systolic murmur with a doubtful diastolic element was present in the aortic and pulmonary areas Blood pressure 140/100 Liver was enlarged up to the level of the umbilicus Moist sounds were heard at both the bases of the lungs There was no oedema anywhere Urine showed albumin and a few hyaline casts Blood Wassermann strong positive Weight 94 lbs Radiological examination of the

heart on 11-10-46 showed enlargement of the heart both towards the right and left, ventricular hypertrophy, prominent pulmonary conus, and enlargement of the left auricle in the right anterior oblique view with barium in the oesophagus. Right transverse diameter of the heart 2.4 inches, left 4.2 inches, total transverse diameter 6.6 inches, total diameter of the chest 9.9 inches. Electrocardiogram on 11/10 (fig 5) showed auricular fibrillation diminished R in Lead I and prominent R and S in Leads II, III and IV, indicating hypertrophy of both the ventricles.

The patient was put on digitalis and diuretics by mouth and vitamin B complex by injections. Signs of congestive heart failure disappeared but auricular fibrillation still persisted.

Digitalis was stopped and quinidine was started on 11th with a test dose of 5 gr. On 12th the patient had 5 gr, and on the 13th morning auricular fibrillation disappeared. Auscultation of the heart now revealed a diastolic murmur in the aortic and pulmonary areas with well defined systolic murmur at the base, indicating aortic stenosis and regurgitation. Electrocardiogram on 15/10 (fig 6) showed regular sinus rhythm with a P-R interval of 0.16. From the 13th to the 22nd the patient had 5 gr of quinidine a day except for 3 doses of 5 gr each (15 gr) on the 15th. The quinidine was stopped on 23-10-46 after a total dose of 70 gr. Digitalis was again started and continued up to 14-11-46 and stopped. The patient felt considerably better, the heart remained regular but tachycardia after slight exertion still persisted. The patient is still in the hospital.

Case (4) R. A., male aged 35 years, was admitted on 1-11-46 with a history of breathlessness and palpitation of 3 years' duration. The patient was married, had 5 children, all healthy. The palpitation has been more severe for the last one month.

Physical examination showed a well built individual, not anaemic, with no cyanosis, no clubbing of the fingers. Heart apex beat in the 6th intercostal space 2 inches from the mid-clavicular line, right border 1 inch external to the right lateral sternal line. Auscultation revealed a systolic murmur in the mitral area and a faint systolic murmur in the aortic area. Heart was irregular and showed auricular fibrillation. Blood pressure 114/74. Liver was enlarged and slightly tender. Lungs showed a few moist sounds at the bases. Urine normal. Radiological examination on 6-11-46 showed enlargement of the heart both towards the right and left, left ventricular hypertrophy, prominent pulmonary conus and left auricle could be visualised in the right anterior oblique view with barium in the oesophagus. Right transverse diameter of the heart 2.2 inches, left 3.9 inches, total 6.1 inches, transverse diameter of the chest 10.1 inches. Electrocardiogram on 1-11-46 (fig. 7) showed auricular fibrillation, W shaped QRS complex in Lead I and prominence of R and S in Leads II and III.

The patient was put on digitalis, diuretics and bromides. Signs of congestive heart failure disappeared but auricular fibrillation persisted. On 7-11-46 the patient was given totaquina 5 gr 3 times a day. This was continued the next day, auricular fibrillation was not con-



Fig 1 (Case 1) taken on 27-8-46 Leads I, II and III showing auricular fibrillation and right axis deviation

Fig 2 (Case 1) taken on 14-10-46 Leads I, II and III showing normal rhythm after quinidine therapy Right axis deviation is present

Fig 3 (Case 2) taken on 11-10-46 Leads I, II and III showing auricular fibrillation

Fig 4 (Case 2) taken on 15-10-46 Leads I, II and III after quinidine therapy fibrillation has disappeared arrhythmia is clearly seen in Leads II and III

Fig 5 (Case 3) taken on 11-10-46 Leads I, II and III showing auricular fibrillation It is small in I and II R and S are prominent in Leads II and III

Fig 6 (Case 3) taken on 18-10-46 showing normal rhythm after 10 gr of quinidine

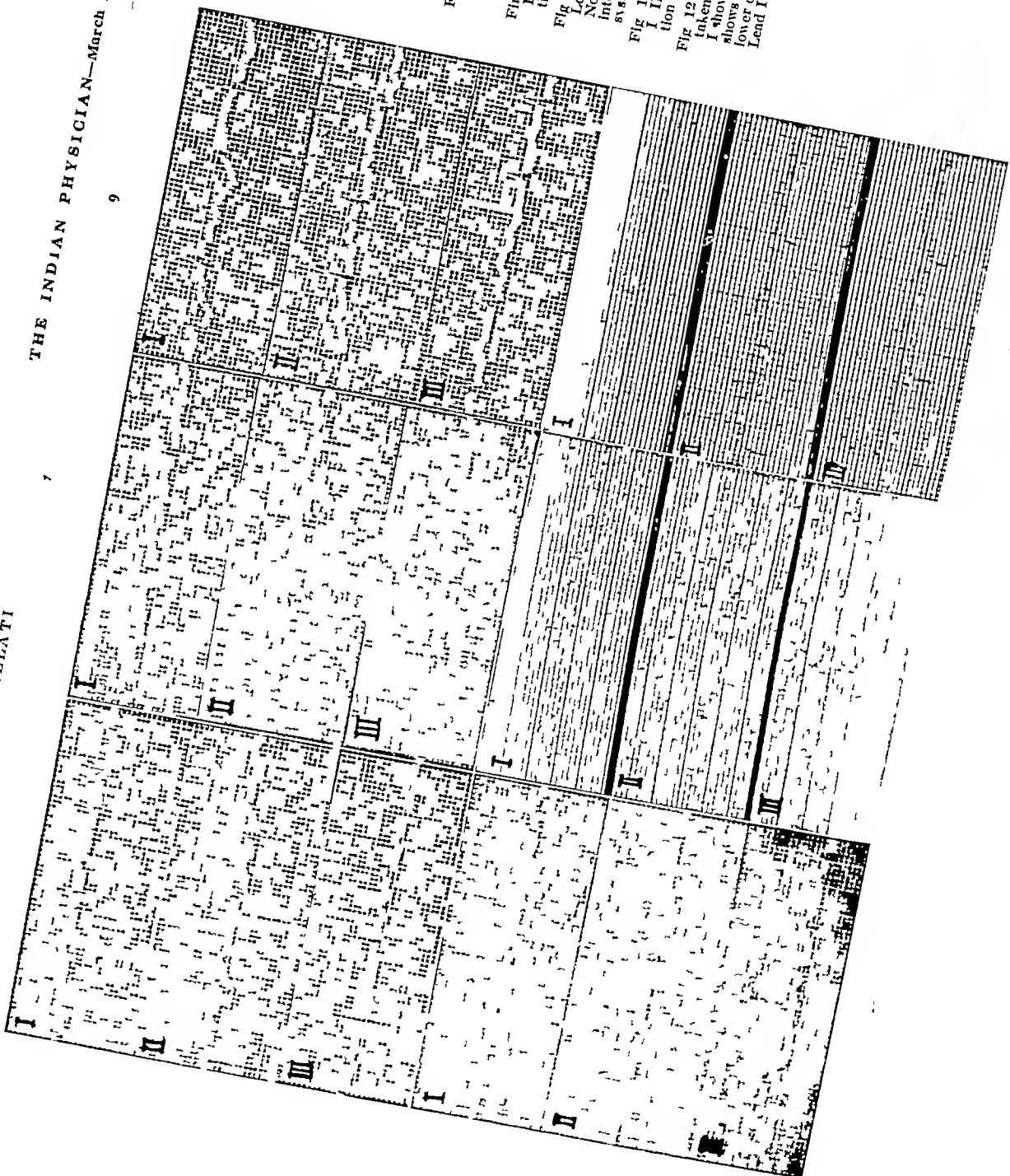


Fig 7 (Case 4) taken on 11-46 Leads I II and III showing auricular fibrillation
 Fig 8 (Case 4) taken on 12-46 Leads I II and III after quinidine therapy has reached the maximum of 0.2 sec
 Fig 9 (Case 5) taken on 17-46 Leads I II and III showing auricular fibrillation and right axis deviation
 Fig 10 (Case 5) taken on 24-46 Leads I II and III after quinidine interval 0.2 sec One ventricular extrasystole is present in Lead III
 Fig 11 (Case 7) taken on 1-41 Leads I II and III showing auricular fibrillation taken on 5-41 Leads I II and III shows normal rhythm Lead II, middle lower one taken 5 minutes after previous Lead II showing positive P

trolled and the dose of totaquina was increased to 30 gr a day. On the 11th auricular fibrillation was still persistent and the patient was given 1/60 gr of strychnine hydrochloric morning and evening. On the 12th auricular fibrillation disappeared and auscultation revealed a definite diastolic murmur in the 3rd left intercostal space indicating aortic regurgitation. Pulse became regular 70 per minute. Electrocardiogram on 12-11-46 (fig 8) showed regular sinus rhythm and the same QRS complex in Lead I was present. Strychnine hydrochloride 1/60 gr was continued morning and evening. On the 13th the same dose of totaquina was continued but strychnine was stopped. Electrocardiogram on 13/11 showed the same picture. On the 14th morning at 7-30 a.m. the patient felt a little bit uneasy, collapsed and died 5 minutes later. Postmortem was not available.

2 Myocarditis, pulmonary hypertension

Case (5) R. A., male aged 50 years, was admitted on 29-5-46 with a history of chronic bronchitis and dyspnoea of 1½ years' duration. He used to get occasional attacks of fever with rigour. He was not addicted to alcohol.

Physical examination showed a moderately nourished individual with general anasarca, cyanosis, prominent jugular veins and enlargement of the liver indicating moderate degree of congestive heart failure. Heart was enlarged, left border 2 inches external to mid-clavicular line, right border right lateral sternal line. Auscultation showed a faint systolic murmur in the apex. Auricular fibrillation was present with a pulse deficit of 12. Blood pressure varied from 146 to 150 systolic and 84 to 100 diastolic. Electrocardiogram on 20-6-46 showed auricular fibrillation and right axis deviation. Lungs showed emphysema and moist sounds all over.

The patient was put on digitalis and diuretics by mouth and mersalyl injections once a week. The signs of congestive heart failure disappeared but auricular fibrillation persisted, and he was discharged relieved on 28-6-46.

He was readmitted on 12-8-46 with the same physical signs but signs of congestive heart failure were more pronounced. Blood pressure was 110/75. He was given digitalis and diuretics and mersalyl as before. Congestive heart failure symptoms disappeared but auricular fibrillation persisted. Radiological examination on 18-8-46 showed enlargement of the heart both towards the right and to the left and prominent pulmonary conus. Right transverse diameter of the heart 24 inches, left transverse diameter 41 inches, total transverse diameter 65 inches, transverse diameter of the chest 10.9 inches. Digitalis was continued up to 11-10-46.

Treatment with quinidine was started on 12/10 with a test dose of 5 gr and had on the 14th 5 gr twice a day, 15th 5 gr 3 times a day, 16th and 17th 5 gr a day. Electrocardiogram (fig 9) on 17th showed no toxic effects with quinidine but only auricular fibrillation with right axis deviation. As the fibrillation still persisted quinidine was continued i.e. 15 gr a day on 18th, 19th and 20th, 21st and 22nd it was increased to 25 gr a day. Auricular fibrillation was not con-

trolled So 1/60 gr of strychnine hydrochloride was given twice a day in addition On 23rd morning auricular fibrillation was present but disappeared in the afternoon and electrocardiogram confirmed the diagnosis 30 gr of quinidine and 1/60 gr of strychnine hydrochloride morning and evening were continued Another electrocardiogram (fig 10) on 24-10-46 showed regular sinus rhythm and prolongation of P-R interval to the maximum of 0.2 of a second Lead III showed ventricular extra-systoles

The patient had 165 gr of quinidine in eleven days with 1/60 gr of strychnine hydrochloride for 2 days and this controlled the auricular fibrillation Afterwards the patient had a maintenance dose of quinidine 5 gr a day up to the 4th and the drug was discontinued afterwards Heart remained regular varying between 60 to 80 per minute The patient felt considerable improvement, his palpitation disappeared and he was discharged on 20-11-46

3 *Exophthalmic goitre*

Case (6) B J R, male aged 37 years, was admitted on 23-5-40 with a history of goitre, nervousness, palpitation and emaciation of six years duration Palpitation was more prominent for the last two years He was married, had 3 children, 1st child died and last child was aged 6 years

Physical examination showed an emaciated individual with exophthalmos and prominent goitre There was no oedema, no cyanosis Heart was enlarged, left border in the left mid-clavicular line, right border in the right lateral sternal line Pulse was irregular and auscultation showed auricular fibrillation with pulse deficit of 12 A faint systolic murmur was present in the mitral area Blood pressure 98/70 Respiratory and alimentary systems were normal Radiological examination on 6-6-40 showed enlargement of the heart The patient had a low fever between 99 and 100° F Weight 70 lbs Urine normal Blood cholesterol 139 mg per 100 cc of blood Glucose tolerance test done on 24-6-40 showed slight hyperglycemia and glycosuria

		Blood sugar	Urine sugar
1	Before glucose	96 Mg	Nil
2	$\frac{1}{2}$ hr after 32 g of glucose	200	Nil
3	1 hr	238	+
4	1½ hrs	113	+
5	2 hrs	87	Specimen not available

The patient was put on Tr digitalis 10 m 3 times a day and the rate was controlled Pulse deficit was still present On 18/7 digitalis was stopped and he was put on iodine Since the auricular fibrillation was not controlled, the patient was transferred to the surgical wards for the removal of the thyroid Subtotal thyroidectomy was done on 21-8-40 by Dr R Mahadevan, and the section of the gland under microscope showed diffuse adenomatous goitre of the macro-follicular type

The patient was transferred back to the medical wards on 5-9-40 with persistent auricular fibrillation Electrocardiogram on 11/9 confirmed the diagnosis of auricular fibrillation The patient went home

for a few days and returned on 12/10 for further treatment. The auricular fibrillation was still present in spite of the removal of the thyroid gland. Heart was enlarged and blood pressure was 90/50.

Quinidine was started on 13/10 with a test dose of 3 gr. On the 14th and 15th he had 5 gr twice a day. On the 16th the auricular fibrillation stopped, the pulse became regular, 70 per minute but a few ventricular extrasystoles were present. In this case 23 gr of quinidine controlled the auricular fibrillation and it was not continued further. Rhythm remained normal afterwards, and he was discharged on 29-10-40. He could not be followed further.

Case (7) N. K., male aged 45 years, was admitted on 18-4-41 with a history of palpitation and dyspnoea of 6 years duration. He gave a history of syphilis, was married, wife died, and had only one son. An operation of ligation of the superior thyroid arteries was done by Dr M. G. Kinn on 19-3-40 for exophthalmic goitre with auricular fibrillation and congestive heart failure. Physical examination showed an emaciated individual with exophthalmos, goitre, prominent pulsating arteries, enlarged liver and enlarged heart with left border 1 inch external to the mid-clavicular line, right border just external to right lateral sternal line. Systolic murmur was heard in the mitral area, conducted towards the axilla, and systolic murmur with accentuated 2nd sound was heard in the pulmonary area. Auricular fibrillation was present. Blood pressure 108/80. Urine showed a trace of albumin. He was discharged on 25-4-41.

He was readmitted on 1-7-41 with signs of congestive heart failure and auricular fibrillation with a pulse deficit of 10. Electrocardiogram on 1-7-41 (fig 11) showed auricular fibrillation, negative T in Leads II and III and prominent fibrillary waves in Lead III. Quinidine was started on 1-7-41 with a test dose of 3 gr. On the 4th, the patient had 5 gr twice a day, and on the 5th 5 gr at 7 o'clock in the morning. At 10 a.m. auricular fibrillation disappeared. 10 more grains of quinidine was given on the same day and it was stopped. Electrocardiogram on 5-7-41 (fig 12) showed normal rhythm, P was inverted in Lead II, in another electrocardiogram taken 5 minutes later on the same day P became erect. On the 8th, auricular fibrillation reappeared. Quinidine was started again, 5 gr twice a day. The next day normal rhythm was restored, a few ventricular extrasystoles were present. 5 gr of quinidine 3 times a day was continued. In spite of continued administration of quinidine, auricular fibrillation reappeared on the 12th. The patient refused to remain any more in the hospital and was discharged on 13-7-41. He could not be followed further.

In case (1) 38 gr of quinidine controlled the auricular fibrillation. Quinidine was continued until the patient had 158 gr and normal rhythm was restored for 53 days. Auricular fibrillation reappeared, remained only for 2 days and 15 gr of quinidine controlled the relapse. Normal rhythm continued till he was discharged from the hospital. In case (2) auricular fibrillation was controlled by 18 gr of quinidine and rhythm remained normal for 14 days. A maintenance dose of 5 gr was continued until the patient had 55 gr. It was stopped.

for 3 days, and auricular fibrillation reappeared 5 gr of quinidine again controlled the auricular fibrillation. A maintenance dose of 5 gr a day was given for 5 days after the 2nd attack of auricular fibrillation. Normal rhythm was restored and it persisted till the discharge of the patient from the hospital. In case (3) of mitral and aortic lesion, 10 gr of quinidine in 2 days controlled the auricular fibrillation. The quinidine was continued for another 10 days with a total of 70 gr. Normal rhythm was restored and the patient felt considerably better except for slight tachycardia on exertion. Case (4) of mitral stenosis and aortic regurgitation was treated with digitalis and later put on totaquina since quinidine was not available. 90 gr of totaquina with digitalis had no effect on the auricular fibrillation, so strychnine hydrochloride injections were given in addition and another 30 gr of totaquina controlled the auricular fibrillation. The patient died 48 hours after the rhythm became normal. Postmortem was not available. The cause of death in this patient could not definitely be ascertained. Clinically there was no evidence of embolic phenomena.

In case (5) of myocarditis with pulmonary hypertension and congestive heart failure of more than 4 months' duration, the dose of quinidine had to be increased till 25 gr were reached for a day. Since auricular fibrillation was not controlled, the dose was further increased to 30 gr a day (10 gr t.d.s.) with 1/60 gr of strychnine hydrochloride morning and evening in addition. 165 gr of quinidine in 11 days with strychnine for 2 days controlled the auricular fibrillation. A few ventricular extrasystoles were present for 3 days after normal rhythm was restored. A maintenance dose of 5 gr a day was continued for 10 days and then stopped. The patient considerably improved and rhythm remained normal (24 days) till he was discharged from the hospital. He had on the whole 215 gr of quinidine. The patient was asked to report once a month to watch the progress.

Case (6) had thyrotoxicosis and exophthalmic goitre for 6 years, but the total duration of auricular fibrillation could not be stated with certainty. He was treated with digitalis and iodine for 4 months, then subtotal thyroidectomy was done. Auricular fibrillation still persisted for another 2 months, then quinidine was started and 23 gr controlled the auricular fibrillation which was persistent for more than 6 months. Case (7) had thyrotoxicosis and exophthalmic goitre for 7 years. He had congestive heart failure in addition. Digitalis, iodine and ligation of the superior thyroid arteries had no effect on the auricular fibrillation which persisted for 16 months after our first observation. 18 gr of quinidine controlled the auricular fibrillation. The drug was stopped for 2 days, fibrillation reappeared, and 10 gr of quinidine once more controlled the fibrillation in 24 hours. Normal rhythm occurred for 3 days but fibrillation reappeared in spite of the fact that the patient had 15 gr of quinidine daily for 3 days. He had a total of 98 gr of quinidine in 8 days.

Pharmacological and therapeutic action of quinidine

Quinidine, one of the alkaloids of cinchona bark, is the dextroisomer of quinine. Quinidine sulphate, the salt commonly used, is a white crystalline substance readily soluble in water. It is absorbed by the small intestines and is rapidly eliminated, usually in 4 hours, by the kidneys. When given intravenously, it disappears from blood in 5 minutes.

Experiments on anaesthetised animals showed slowing of the impulses from the sino-auricular node, increase in P-R interval, delayed intraventricular conduction and increase in the refractory period. In animals not anaesthetised, delayed intraventricular conduction was the only abnormality observed (Smith and Boland).

In therapeutic doses, it increases the refractory period and thereby decreases the excitability of the myocardium, increases the force of contraction, slows the rate of the heart, slows the rate of conduction, and irregular rhythm is made regular (Goodman and Gilman). Of these increase in the refractory period and decrease in the conductivity are the two main actions and both are opposed, usually one action is predominant over the other. If increase in the refractory period is the main action, the auricular fibrillation stops, but if decrease in the conductivity is the predominant action, fibrillation still persists. The action of quinidine is mainly on the myocardium and closes the gap in the circus movement that is present in cases of auricular fibrillation.

Mode of administration—Different authors advocate different methods for the administration of quinidine, but all start with a test dose of 1½, 3 or 5 gr and if no untoward symptoms occur, the drug is continued the same day or the next day in increasing doses. Weisman (loc cit) recommends the following line of treatment—

1st day 1½ gr
2nd day 3 gr (1½ gr every 2 hours)
3rd day 6 gr (1½ gr every 2 hours)
The same dose is continued up to the 7th day
8th day 20 gr (5 gr every 2 hours)
9th day 30 gr (10 gr every 2 hours)
10th day 40 gr (10 gr every 2 hours)

As soon as normal rhythm is restored, the dose is reduced to 5 or 10 gr a day either daily or on alternate days, and during the first 3 days the patient gets digitalis in addition, but in some cases it is continued along with the quinidine.

East and Bain give after a test dose of 5 gr of quinidine 30 grs (5 grs every 2 hours) next day, and if normal rhythm occurs it is stopped, or the dose is continued for the next 2 days if normal rhythm is not restored. The drug is then stopped and the patient is put on digitalis till the pulse rate comes down to 80. They then give 30 gr of quinidine every day for 3 days. If the fibrillation still continues, a 3rd course is given, and if that too does not succeed, the attempt is given up. Parkinson and Campbell (loc cit) recommend 5 gr in the first day and the dose is increased daily, increasing up to 10, 20 and 30 gr a day, and this maximum dose is continued for 3 days until normal rhythm is restored. Levine (loc cit) recommends 0.2 gr twice a day on the first day, then 0.3 gr 3 times a day, and then the dose is

increased to 0.4 and 0.5 gr a day until the desired effect is produced. The dose is reduced immediately the rhythm comes to normal. Goodman and Gillman (loc cit) recommend 0.4 gr five times a day every 4 hours (30 gr a day) and is continued for 10 days and according to them constitute one course of quinidine. The drug is stopped immediately toxic reactions occur.

In the present series, after a test dose of 3 or 5 gr the patients had 15 gr (5 gr t.d.s.) and if auricular fibrillation was not controlled, the dose was increased to 25 and later to 30 gr a day. Two cases required strychnine in addition. When more than one dose was given, it was administered every hour or every 2, 3 or 4 hours, or 3 times a day. The administration of the drug every hour seemed to have a better effect than the other methods of administration. The best result is obtained when the drug is administered every 2 hours (Wolff and White).

The total dose of quinidine necessary to stop the fibrillation varies in different cases. A test dose of 3 gr once controlled the auricular fibrillation (Brill). Smith and Boland used doses varying from 10 to 2620 gr, on an average 60 gr to control the auricular fibrillation. The last case that had 2620 gr seems to be exceptional, and this patient had an average of 40 gr a day. In the present series of the authors, the doses that controlled the auricular fibrillation were 10, 18, 18, 23, 38, and 165 gr during a period of 2, 3, 3, 3, 3, and 11 days respectively. One patient had totaquina of 120 gr in 5 days. Wolff and White (loc cit) in their series used more than 100 gr of quinidine in 8 cases and less than 100 gr in 36 cases and of these 28 cases required only 50 gr or less to control the auricular fibrillation. The total duration of treatment was one day in 5 cases, 2 days in 19 and 3 or less in 33 cases.

How long should the drug be continued after the normal rhythm is restored? A maintenance dose of 5 gr or 10 gr daily or on alternate days is recommended for a few days, weeks or according to some authors, for an indefinite period (Levine). In the present series, 5 cases had a maintenance dose of 5 gr a day for 7 to 10 days, and in one case it was stopped after normal rhythm was restored.

Intravenous administration of 3 to 6 gr in 10 cc of water, or 50 gr in 500 cc of normal saline by drip method has been advocated in serious cases (White).

Toxic action

A test dose occasionally shows idiosyncrasy of the patient to the drug, and is manifested by difficulty in, or temporary stoppage of respiration, dizziness, nausea, vomiting, cyanosis or cold and clammy sweats. Toxic reactions such as headache, tinnitus, vertigo, dimness of vision, tachycardia, embolic phenomena, and sudden death by ventricular fibrillation or ventricular stand-still are reported. High fever has recently been observed (Sturnick). In the present series, there was only one doubtful case in which toxicity can be attributed to quinidine. In this patient, death occurred after 180 gr of totaquina. No other toxic symptoms were observed in any of the other cases.

Caffeine has been recommended as the best antidote (Clendenning and Hashinger)

Tachycardia—When tachycardia occurs, it is due to slowing of the auricular rate which permits the ventricle to respond to every auricular beat (East and Bain) When it is regular it might be sinus tachycardia or auricular flutter Warren (1936) found auricular flutter in 14.8 per cent of 263 cases and Smith and Boland in 9.7 per cent of 41 cases treated with quinidine and in one case of the latter it persisted for 66 days Normal rhythm may be restored or fibrillation might be re-established after varying intervals Paroxysmal ventricular tachycardia also has been observed (East and Bain)

Embolic phenomena—Levy (1922) observed embolism in 5 of 25 cases treated without quinidine and only one in 25 treated with quinidine Viko et al (1923) collected from the literature 484 cases of auricular fibrillation treated with quinidine and compared the results with 200 cases in which quinidine was not given, and concluded that quinidine therapy did not increase the incidence of embolic phenomena Carr (1924) did not observe even a single case of embolism in 75 cases treated, although 23 regained normal rhythm Hay (1924) reported 7 cases of embolism that occurred 3 hours to 8 days after normal rhythm was restored in a series of 286 patients treated with quinidine Weisman (1932) observed only one case of hemiplegia of the right side in a woman of 37 which might be attributed to embolism Smith and Boland (1939) in a series of 41 cases observed embolic phenomena in 6 cases but all of them occurred before quinidine treatment was started Askey (1946) from a statistical study found that the risk of embolism was only 4 per cent when quinidine is given, but it was far greater (15 to 25 per cent) if auricular fibrillation was allowed to continue without quinidine He says embolic phenomena do occur in cases of auricular fibrillation even without any quinidine and if the irregularity is allowed to continue the clot in the auricle may increase in size and thereby increase the incidence of embolic phenomena, whereas the risk of embolism is present only for a few days after the normal rhythm is restored in cases treated with quinidine

The senior author has come across 5 cases of hemiplegia which may be attributed to embolic phenomena, in patients suffering from mitral stenosis, but in all these cases there was no auricular fibrillation at the time of examination In two other cases of auricular fibrillation death occurred and postmortem in one case revealed a ball thrombus in the left auricle, and in the other multiple thrombi in both the auricular appendices There was no evidence of embolic phenomena These cases will be dealt with in detail in another communication

Sudden death—When a patient dies during the course of quinidine therapy, death is usually attributed to that drug, but it has been proved by postmortem that the majority of the patients have died of some other cause Hay (1924) reported 8 deaths from a series of 286 cases out of which one was certainly not due to quinidine Wolff and White (1929) reported only one doubtful case in 91 cases of per-

manent or paroxysmal auricular fibrillation Parkinson and Campbell (1929) observed 4 per cent of deaths in a series of 554 patients Levine (1936) reported 3 deaths and these on postmortem examination did not show any embolus or thrombus Smith and Boland (loc cit) reported 3 deaths in a series of 41 cases, and autopsy in 2 of these cases showed enlarged and dilated heart and sclerosis of the coronary vessels There was no evidence of coronary thrombosis and there were no clots either in the auricle or ventricle Askey (1946) from the literature analysed 29 cases of auricular fibrillation, 16 with and 13 without congestive heart failure, treated with quinidine

Sudden death occurs in all forms of heart disease with or without auricular fibrillation and even in cases of auricular fibrillation with or without administration of quinidine Cookson (1930) reported 86 deaths, out of which sudden death occurred in 9 cases Postmortem, which was available in 2 cases only, could not ascertain the cause of death Cardiac standstill, ventricular fibrillation or respiratory paralysis have been attributed as the cause of death in these cases Levine (1936) from animal experiments found respiratory paralysis as the main cause of death and concluded artificial respiration and caffeine could save the life in such cases In the present series of the authors, only one patient died (case 4), and in that case it was sudden At 7 a.m. in the morning he got giddy and died 5 minutes later He had no quinidine but only 150 gr. of totaquina which contained quinidine Death in this case occurred 48 hours after normal rhythm was restored Postmortem was not available to ascertain the exact cause of death

Indications and contra-indications—The drug is indicated (1) in young individuals with very slight damage to the heart muscle, (2) in whom the auricular fibrillation is of recent origin, (3) in cases of persistent auricular fibrillation after thyroidectomy, (4) in intractable cases when palpitation is severe, and (5) in cases where all other methods of treatment have failed (Goodman and Gillman) The drug is also given as a prophylactic in cases of rheumatic heart with auricular extrasystoles to prevent the development of auricular fibrillation (Levine)

The common contra-indications are (1) idiosyncrasy, (2) congestive heart failure, (3) acute infectious fever or subacute bacterial endocarditis, (4) long duration, (5) embolic phenomena, and (6) gross myocardial damage White (1944) says that quinidine reduces the incidence of embolic phenomena in cases that have already suffered from embolism and is life saving in certain cases who are dangerously ill with extreme tachycardia and congestive heart failure not amenable to digitalis Recently Askey (1946) stated that the dangers of quinidine were over-emphasised and it is life saving in some patients with congestive heart failure, long-standing auricular fibrillation and conduction defects, and should be given a fair trial in patients who are desperately ill He collected 13 cases from the literature and added 2 more of his, who were desperately ill with auricular

fibrillation and congestive heart failure or embolic phenomena and who responded well to quinidine

Factors affecting the success or failure of quinidine therapy

Success or failure of treatment of auricular fibrillation by quinidine depends on age, aetiological factor, duration, size of the heart, ventricular rate, inter-current infection or alcoholism and the use of digitalis and strychnine before or during the administration of quinidine

Recent observations by Askey have made us try quinidine in every case of auricular fibrillation that was admitted. The two cases of 'thyrotoxicosis with exophthalmic goitre' were treated 5 years ago. During the year (1946), 6 patients with auricular fibrillation were observed by the senior author, out of which the treatment with quinidine was withheld only in one patient since there was considerable enlargement of the heart with gross myocardial damage, as shown by clinical, radiological and electrocardiographic findings

Age and sex—The minimum age in this series was 25 and the maximum was 55 years. There were 5 males and 2 females. In all cases fibrillation was controlled but relapse occurred in 3, and in those normal rhythm was again restored after a second course of quinidine. In one case, the patient left the hospital with persistent auricular fibrillation. The high percentage of success reported in younger individuals could be explained by the greater incidence of rheumatic heart in that age group. The oldest man in this series required the largest dose and the longest interval for normal rhythm to be restored.

Aetiology—Four of the cases belonged to the rheumatic group, two to thyrotoxicosis and exophthalmic goitre, and one to myocarditic with pulmonary hypertension. In both the cases of thyrotoxicosis, quinidine was used because fibrillation could not be controlled even by the operative procedure of subtotal thyroidectomy or ligation of the superior thyroid arteries. In case (7) fibrillation was controlled but reappeared again. Wolff and White (loc cit) classified these cases under 4 headings, and according to them there is no significant variation in the response to quinidine in the various groups, viz, (1) rheumatic, (2) hypertensive and arterio-sclerotic, (3) hyperthyroid, and (4) normal hearts.

Duration and the presence of congestive heart failure—The duration of auricular fibrillation could not be stated with certainty in any of the cases but it can safely be said that it lasted for more than 6 months in one case (No 6), 1 year in another case (No 3), and 16 months in the third (No 7). In the first two, the fibrillation was controlled, but in the 3rd it reappeared and the normal rhythm could not be re-established in spite of continued administration of quinidine. Congestive heart failure was present in all the cases except in one case (No 6) of thyrotoxicosis and exophthalmic goitre.

Size of the heart—The size of the heart in the present series was measured from the radiograms taken at 2 metres distance.

Case No	Rt Transverse	Lt Transverse	Total Transverse Diameter	Transverse diameter of the chest	Cardio-thoracic ratio
1	1 5"	4 2"	5 7"	9 0"	0 64
1 after treatment	1 4 3/4"	3 7"	5 1 1/2"	9 8"	0 52
2	1 0"	3 5"	5 4"	9 2"	0 58
3	2 4"	4 2"	6 6"	9 9"	0 60
3 after treatment	2 4"	3 8"	6 2"	9 9"	0 62
4	2 2"	3 0"	6 1"	10 1"	0 60
5	2 4"	4 1"	6 5"	10 0"	0 59

A second radiological picture was taken in cases 1 and 3 and showed reduction in the size of the heart. This is the usual finding that is present in any case of congestive heart failure and might not have anything to do with quinidine therapy.

Big sized hearts were present in three cases, two showing involvement of the aortic valves and the 3rd with myocarditis and pulmonary hypertension. The largest size of the heart was observed in case (3) and he responded with the smallest dose of 10 gr of quinidine. The relative size of the enlarged heart probably has no relation with response to quinidine therapy. Wolff and White (loc cit) observed that normal rhythm was restored in 100 per cent of normal hearts, 57.5 per cent with slight enlargement, and 63.1 per cent with marked enlargement.

Digitalis and quinidine—All cardiologists are now agreed on the necessity of preliminary administration of digitalis in all cases of auricular fibrillation before quinidine therapy is started, but whether it must be continued along with quinidine, there seems to be difference of opinion. All our patients had digitalis before quinidine was started, and it was continued only in one case (No 3) after the quinidine was stopped, because tachycardia was still persistent. Digitalis was not given simultaneously in any of the cases. Cantani (1905) reported favourable results of quinidine on the action of digitalis. Schott (1920) found auriculo-ventricular block in experimental animals and found that it was not safe to administer digitalis and quinidine simultaneously. Wolff and White (loc cit) failed to observe undesirable effects and found that the most favourable results were obtained when digitalis was given in doses big enough to produce negative T in Leads I and II. Askey and Neurath (1945) found from an analysis of 84 cases of auricular fibrillation in association with myocardial infarction, that normal rhythm was restored in 5 out of 17 cases without any medication in 9 out of 11 cases treated with quinidine alone, in 6 out of 44 with digitalis alone, and in 9 out of 12 with digitalis and quinidine.

Strychnine and quinidine—Smith and Boland (1930) found that strychnine supplemented the action of quinidine in the treatment of auricular fibrillation and used 1/40 to 1/30 gr of strychnine sulphate 3 times a day by injection and observed that normal rhythm was restored in 80.4 per cent of 41 cases. Two of our patients were given strychnine hydrochloride 1/60 gr morning and evening and this method was resorted to because the rhythm was not controlled either by totaquina or quinidine. Normal rhythm was restored in both the cases within 24 to 48 hours.

Should quinidine be given to all cases of auricular fibrillation to bring the rhythm to normal? Some patients feel considerable improvement, some show slight improvement and in others there is no beneficial effect. One of our patients (No 3) was able to make out the decided difference between the auricular fibrillation which he had for one year and normal rhythm that occurred after the administration of quinidine. Now and then when he gets an attack of sinus tachycardia he can definitely make out the difference between this tachycardia and the auricular fibrillation which he had before. Levine (1936) observed that a slow irregular heart can maintain a better circulation than a rapid and a regular one. Taking all facts into consideration he has come to the conclusion that it is better to have a regular rather than an irregular heart. In the present series, cases 3, 4, 5 and 6 had all very large hearts and case 6 had in addition auricular fibrillation of more than 16 months duration, all contra-indications for quinidine therapy. Of these, two cases showed definite improvement, one died and the other left the hospital with persistent auricular fibrillation.

SUMMARY

(1) Seven cases of auricular fibrillation consisting of rheumatic heart disease 4, thyrotoxicosis 2, and myocarditis with pulmonary hypertension 1, were treated with quinidine.

(2) Normal rhythm was restored in all, but relapse occurred in 3 cases, after 2, 14 and 53 days and normal rhythm was again restored in the last two after 48 hours. Five patients felt considerably better.

(3) In both the cases of thyrotoxicosis and exophthalmic goitre, quinidine was given only after subtotal thyroidectomy or ligation of the superior thyroid arteries.

(4) Sudden death occurred after 150 gr of totaquina, in one case of rheumatic heart with mitral stenosis and aortic regurgitation, 48 hours after normal rhythm was restored.

(5) Pharmacological, therapeutic and toxic actions with indications and contra-indications of quinidine therapy are discussed.

(6) Synergic action of quinidine and strychnine was observed in two cases.

(7) The accidents after quinidine are usually over-emphasised and the drug can be safely given to patients with larger hearts and to those having auricular fibrillation of long duration with considerable benefit to the patient.

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SOME PRACTICAL APPLICATIONS OF ELECTROCARDIOGRAPHY

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The selection of cases, referred for electrocardiographic examination, shows that some practitioners do not evaluate properly what this method is meant for, what an electrocardiogram (e c g) does tell and what it does not

The history of electrocardiography shows great changes in the clinical use of the e c g. For many years, roughly from 1903 to the early twenties, e c gs were traced almost exclusively to elucidate and differentiate various kinds of arrhythmias (*Einthoven*, 1903, *Rothberger & Winterberg*, 1909, *Lewis*, 1909), a line of research which interested more physio-pathologists than clinicians. Therefore, and because of the mathematical difficulties which the analyzing of such graphs presented, the great majority even of progressive medical men shunned the cardiograph chamber as if it were a place for performing black magic. Later on, when electrocardiography was introduced in the investigation of myocardial lesions (*Pardee*, 1920), which now-a-days is its main object, some statistical mistakes discredited this method very soon. Many cardiologists will still remember how strong was the faith in the ominous significance of the inverted T₃, how solemnly we pronounced that those unfortunates who presented this feature had not much longer to live and how so many of these doomed ones went on enjoying life in spite of their inverted T, provided it was confined to lead III. However, in course of time such mistakes were rectified and now electrocardiography is one of the most exact clinical methods which, within well recognised limits, often permits to read the history of the heart of a given case backward and forward with remarkable certainty, its results are as reliable as those of a lung film which says a good deal of past, present and future of a tuberculous infection.

How important it is that an e c g *elucidates the past* of a patient's cardiac history is illustrated by an experience we had recently. A lady educationalist was extremely worried about her professional and personal future because of an attack she suffered some four months ago, diagnosed at a university city as a coronary thrombosis, she had been kept in bed for two months and prevented from joining her duties since then. The e c g, taken now showed flat positive T₁, 2, 4 and an iso-electric T₃ but normal conduction time, normal S-T segments and, especially, no coronary T in any of the leads (fig 2). These findings justified the exclusion of a myocardial infarction for the last six months at least, a conclusion confirmed by her first e c g, record-

ed four days after the attack (fig 1) The lady was advised to assume a normal life within reasonable limits, for the last year she is teaching again, driving her car etc, free from any symptoms perhaps because she took the advice to give up smoking. Her wrongly diagnosed coronary thrombosis, most probably due to a coronary spasm due to excessive smoking

Still more regrettable is the opposite kind of case which comes with the history of a single severe attack of pain in the chest or in the upper abdomen, a couple of weeks ago, treated as a gastric or abdominal colic because it developed, for inst, after a heavy meal, the e c g, however, proves beyond doubt the presence of a myocardial infarction. As no rest had been observed in the time, we may be sure that the crucial period for the formation of a firm scar tissue was missed and the sequelae of a permanent infarcted heart muscle will invariably become apparent. The prognosis for such heart invalids, which could have continued an active life if only an e c g had been taken in time, seems rather gloomy. It is steadily increasing in India due to the quickly spreading habit of smoking of living

A difficult question, which faces the practitioner even today, is to present the male characteristic. A man, nearing fifty, in respect of his position as a banker, businessman, industrialist, a doctor or a professional, comes for consultation, worrying about his heart because of slight dyspnoea after a longer speech or a heavier meal, or a disturbance of his sleep which used to be very sound, or, in the last few weeks, there is a post-prandial feeling of oppression in the chest. His blood pressure is about 150/95, fluoroscopy shows a reverse position of the heart, due to pushed up diaphragm. The essential point is the condition of his heart muscle and this can be decided only by the e c g. This might be within normal limits, but traced at rest but show signs of an insufficient blood supply to the myocardium—"coronary insufficiency"—when repeated at a later time. Only if the tracings show no features of myocardial damage. In both of these conditions, such a patient may be certified as fit for work. From nothing worse than overweight and/or psychic tension, a strict diet, regular moderate exercise, care for clear bowels and, perhaps, some bellergal is all such a man requires. On the other hand, an e c g showing early signs of myocardial strain or, in many cases to stop serious developments or, at least, to delay them considerably, Aminophylline, testicular hormone, mustard oil, such as corhormone, which due to their content of adequate amounts of phosphoric acid seem to tone up the myocardium, regulation of digestion, exercise and business or professional activities. In many cases if applied in time, unfortunately, the right moment is missed all too frequently because the earliest possible moment is missed all too frequently because the method for detecting an incipient myocardial deterioration

mindful but show also an undesirable tendency to extend the age of active, strenuous sport activities far beyond the limits which were recognized as safe only a few years ago. Such people of about forty to forty-five, presenting usually a perfect, even athletic physique, consult us not rarely about complaints which we came to know as typical and significant, especially among polo players. At the end of a sharp game the patient feels some heaviness in the chest, a substernal discomfort or a sudden weakness, a "black-out", with or without some giddiness for a few seconds. The whole attack lasts only for a few minutes but is followed by a feeling of fatigue or depression which induces such a man reluctantly to ask for medical advice.

The clinical findings usually are practically normal, as illustrated by the following case. A Rajput of 46, a polo player of international repute and very moderate habits, consulted us (13-2-46) complaining that a few days ago, on dismounting after a polo match, he felt an unpleasant sensation of oppression and slight pain behind the sternum, lasting for a few minutes. His friends persuaded him to seek medical advice, finding him somewhat depressed. The tall broad-shouldered man, who looks much younger than his age, had a regular pulse, rate 92, blood pressure 145/90, clear heart sounds without any accentuation, liver and spleen not palpable, normal red and white blood picture E.S.R. 6/12. On fluoroscopy the left ventricle was very slightly rounded, aorta normal in all standard positions. But his e.c.g. (fig 3) was distinctly pathological. Apart from a low voltage, the conduction time of 0.2 sec, an elevated S-T4 segment, inverted T1, 2 and a deformed T4 proved that his myocardium was considerably damaged, far more than one would have expected from the clinical findings. According to our advice, he gave up polo playing and had a course of 18 minophylline injections which made him feel better than he had felt for a long time. Then followed a period of normal life without exertion and without any medication. When we saw him again (10-12-46), his pulse rate was 80, blood pressure 128/85, liver and spleen not palpable. This time, his subjectively perfect well-being was fully confirmed by the e.c.g. (fig 4), all the signs of a pathological condition of the myocardium had disappeared. Ten months of an almost unrestricted life, differing from his previous one only by avoiding strenuous exercise, and very little treatment were sufficient to restore a badly damaged, overstrained myocardium to normal.

While in the conditions, discussed up to now, the electrocardiogram was used to find out whether the complaints for a patient are due to a myocardial lesion at all, whether an individual, quite recently supposed to be hale and healthy, is a heart patient or not, we have to deal now with pathological processes which are known to damage the myocardium frequently or are bound to involve it sooner or later.

An important example of this kind represents the decision whether a case of *diphtheria* or *rheumatic fever* is fit to leave the bed and to move about. Here, electrocardiography is of the greatest help.

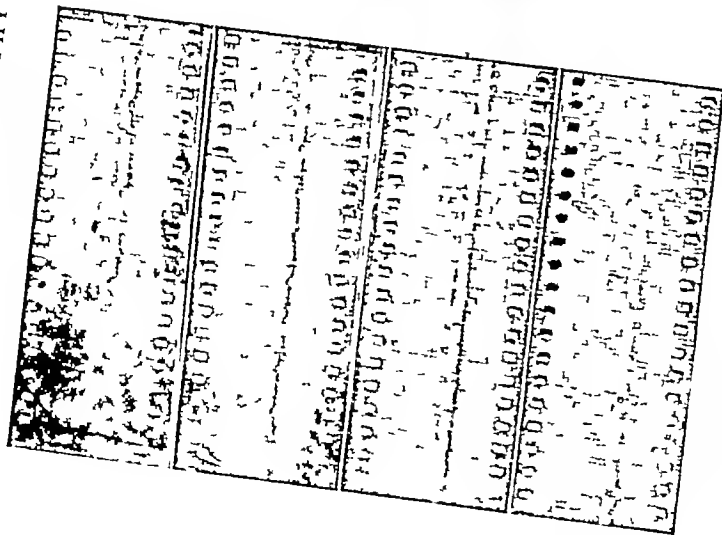


Fig. 1 Four days after pain attack, wrongly diagnosed as coronary thrombosis

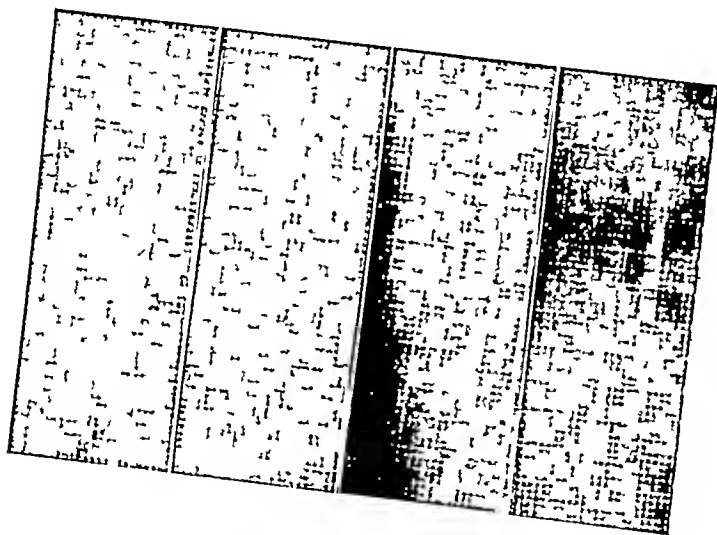


Fig. 2 The same patient, four months later

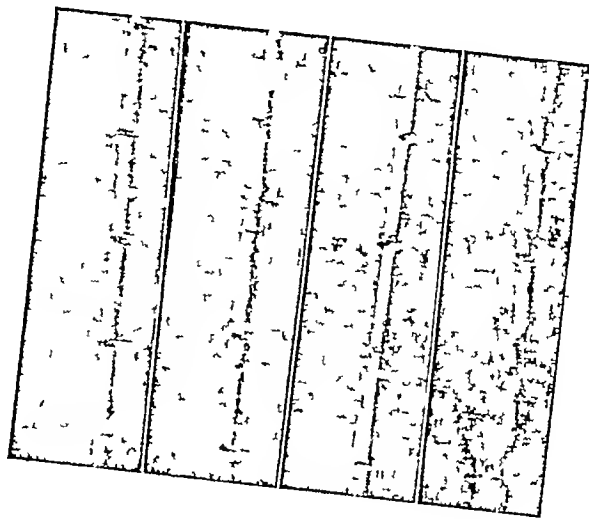


Fig. 3 Myocardial strain due to excessive sport.

unmistakable auscultatory signs long before the e c g shows any alteration. The same is true about a left axis deviation in aortic valvular diseases

On the other hand, toxæmia or anaemia affect so deeply the myocardium and with it the e c g that the tracings of an anaemic young woman with a hypertension due to a nephropathy in pregnancy and those of an ankylostomiasis patient with an extremely low blood pressure look almost alike. The e c g's of both usually show low voltage and absence of T waves without any characteristic feature which would permit to draw diagnostic conclusions. Even the left axis deviation which one would expect in the case of hypertensive nephropathy frequently is missing due to the fact that the coexistent anaemia prevents the development of myocardial hypertrophy.

Figs 5 and 6 illustrate the similarity of e c g's in still more different conditions. Fig 5 belongs to a heavily drinking Rajput, about 50 years of age, 220 pounds body weight, haemoglobin 72 per cent and a blood pressure of 160/110. Fig 6 shows the tracings of a Hindu peasant of 35, 98 pounds body weight, haemoglobin 26 per cent and a blood pressure of 105/65, suffering from ankylostomiasis and malnutrition. Neither of them has got any cardiac complaints and yet, both the e c g's indicate diffuse myocardial damage, characterized by low voltage, more so in fig 6, and absent T-waves, more so in fig 5. The only feature which these two entirely different cases have got in common is the presence of toxic factors: country liquor, which in Rajputana is highly concentrated, in the former, anoxaemia due to anaemia and hookworm toxin in the latter.

It was and still often is discussed whether a stenosis of the mitral ostium is an indication to avoid pregnancy and to interrupt an existing one. It seems that the present condition of the heart muscle as disclosed by an e c g is of greater importance for the maternal forecast than even the state of compensation and the history of past pregnancies. Compensation may change over night, for better or for worse and the past history is of doubtful significance because if previous pregnancies were uneventful, the present one might be just the last straw and if they were accompanied by decompensation, proper treatment could prevent heart failure this time—provided the e c g shows the myocardium to be sound.

The extremely variable symptomatology of coronary occlusion found its common denominator in the e c g which usually a few hours after the onset of the attack shows not only whether pain, collapse, restlessness etc are due to a coronary emergency but if so, also where the infarction is localized. The importance of this diagnostic help cannot be overrated, the whole management of the patient being dictated by it. On the other hand, it is not justified to make the duration of absolute rest following a coronary occlusion dependent on the e c g. In the majority of such cases the electrocardiographic signs of the myocardial scar remain visible much longer than rest is required. The erythrocyte sedimentation rate is a much more sensitive

indicator of the myocardial condition and a far more reliable guide as to what such a patient is permitted to do

The paramount importance of the e c g in the *differential diagnosis of chest pain*, oppression, palpitation, which rarely is of organic cardiac origin, retro- and substernal burning sensation, etc., illustrated by the male climacteric and the middle aged sportsman, is still not sufficiently realized in day-to-day practice. Much suffering, somatic and psychic, could be avoided or, at least, relieved by judicious use of electrocardiography, which in most cases permits to decide whether the complaints originate from the heart and its vessels, whether they are of organic or functional nature, whether the patient requires restriction of his activities, encouragement to carry on in spite of his symptoms or persuasion to lead even a more active life with regular exercise etc to convince him that he is not a heart patient. A normal e c g, recorded at rest and after an exercise test, makes such decisions comparatively easy.

To this group belongs also the *effort syndrome* or neuro-circulatory asthenia which differs from most of the previously mentioned ones by its predominance among young people. It is a mistake to believe that it is confined to soldiers and of interest only to medical men in the forces. Most of the students who are referred to us for heart trouble are suffering from it and, as a rule, turn out to be sexual neurasthenics, all their complaints of palpitation, chest pain, hollowness or heaviness in the chest, attacks of weakness, giddiness etc are only an introduction to interminable descriptions of seminal discharge, night dreams, sensations of heat and cold about the genitals which—in their opinion present all sorts of abnormalities. It is necessary for the understanding of these vasomotor disturbances to see them in connection with these undoubtedly neurotic manifestations. An e c g helps in intelligent patients to convince them that one takes their complaints seriously and to restore their confidence in themselves as, in spite of such investigations, no heart disease could be detected. We refuse to prescribe any placebo in such cases but try to discuss with them their individual difficulties, social, economic or psychological, which invariably form their background. Much goodwill on both sides is needed to come to an understanding without which no success is possible and through which sometimes "miracle cures" are achieved.

The rule that an e c g, showing features of myocardial damage, always connotes an organic lesion does not seem to apply to females suffering from *menopausal trouble*. Such patients frequently describe complaints indistinguishable from angina pectoris, precordial pain, conducted towards the left arm, neck and shoulder, and anxiety dominate the picture. The e c g shows depressed S-T segments in all leads, more so in lead II, and flattening or even inversion of the T-waves. In spite of these serious looking pathological features which under every other condition would be diagnostic of a considerable myocardial lesion, substitution therapy with follicular hormone (ovo-

cyclin, dimenformon, theeline etc) soon controls all the subjective symptoms and after a few weeks eradicates the ominous signs from the e c g Statistics confirm the clinical impression that the frequency of angina pectoris in women is about one tenth of that in men Keeping in mind the existence of this climacteric vasomotor angina, one will be rarely in a position to diagnose organic coronary disease in females

Of the rarer pathological conditions where an e c g substantially contributes to establishing quickly the right diagnosis should be mentioned the *paroxysmal tachycardias* The differentiation between auricular and ventricular tachycardia, of paramount importance for prognosis and therapy, presents no difficulty, once an e c g has been recorded Whereas the former is comparatively harmless and responds almost immediately to prostigmine, the latter is of the most ominous significance, although some cases have been saved by large doses of quinine or quinidine

These few examples, selected almost at random, clearly show that there are many occasions in general practice when the medical man called upon to give a weighty advice or to make a far-reaching decision cannot do so with a clear conscience without knowing what the e c g has to say about the case under consideration This state of affairs, best realized in the U.S.A where in some general hospitals an e c g is traced in every case, has induced many American practitioners to record and analyse e c g's themselves, the consequence is that such amateurs discredit this method in the eyes of the public That is inevitable because it is not enough to boast of an electrocardiograph and to know how to turn the knobs which switch on the motor and change the leads Long experience in reading very many e c g's is required if overlooking of essential features and, still more, the interpretation of harmless variations as pathological changes is to be avoided Great harm was and is done by mistakes in either sense, which certainly are no fault of Einthoven's ingenious invention

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Original Contributions

TOTAL PLASMA PROTEINS

THEIR COMPARATIVE VALUES BY THE SPECIFIC GRAVITY METHOD
OF PHILLIPS ET AL AND BY THE MICRO KJELDAHL METHOD*

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Determination of the plasma proteins is of great value in many pathological conditions of the body. Many attempts are being made to find out a quick and easy method for the quantitative determination of the total proteins.

From the most common standard methods which are used routinely by many clinical laboratories the following can be mentioned —

- 1 Specific Gravity method using the Specific Gravity bottle (Moor and Slyke, 1930)
- 2 Specific Gravity method using falling drops with mixtures of oxylene and bromobenzene (Barbour and Hamilton, 1926)
- 3 Specific Gravity method using falling drops with copper-sulphate solutions (Phillips et al, 1944)

Moor and Van Slyke (1930) have shown that specific gravity and proteins of plasma are directly proportional to each other. The above three methods are based on this principle.

- 4 Micro-Kjeldahl method (Kolmer and Boerner, 1941) This depends upon the relation of the nitrogen content of serum and weight of the proteins.
- 5 Gravimetric method (Guillaumin, 1929) In this method proteins are first precipitated from the plasma by acetone. They are further purified by partially dissolving them in 0.6 per cent sodium chloride solution adjusting pH to 4.7 by adding acetic acid and then coagulating by heat. Finally they are weighed as pure proteins.
- 6 Colorimetric method (Greenberg, 1929)
- 7 Biuret method (Harrison, 1939) These methods Nos 6 and 7 depend upon the colorimetric principles where specific reagents are used.
- 8 Proximate method (Fishberg and Dolin, 1931) This method quantitatively determines the capacity of a sample of serum.

*A paper read at the 73rd meeting of the Teaching Pathologists Bombay, November 1946

to act as a buffering solution and the total proteins estimated therefrom

- 9 Refractometric method (Robertson, 1915) This method depends upon the refractive capacity of serum

Peter and Van Slyke (1932) recommend the gravimetric method for greater accuracy of the results. The Kjeldahl analysis can be done with errors not exceeding 1 per cent. The colorimetric methods are liable to errors upto 10 per cent. Linder, Lunsgaard and Van Slyke (1924) found refractometric deviations from Kjeldahl results as great as 15 gms of total proteins per 100 ccms of plasma. The specific gravity method may give an error of ± 0.6 gms proteins per cent plasma.

Phillips et al (1944) claimed that the falling drops in Copper sulphate solutions method of finding specific gravities of human plasma gave figures for total proteins comparable to micro-Kjeldahl method by ± 0.3 gms proteins per 100 ccms plasma. Atchley et al (1945) stated that in their experience, the method of Phillips et al (1944) proved to be a simple and accurate method for determining plasma proteins.

However, some workers find that the results of plasma proteins obtained by specific gravity methods do not agree with Kjeldahl method. Zozaya (1935 and 1938) found that the values of plasma proteins obtained by specific gravity method do not agree with the real figures. Moon et al (1941) working on similarities and distinctions between shock and effects of haemorrhage did not get concordant results with these two methods. Looney (1942) working on patients with schizophrenia and normal subjects found that specific gravity determinations did not give accurate results. Adams and Ballon (1946) in their determinations of plasma proteins—mostly on cases of burns, state that the correlation between specific gravity of plasma and its protein contents was found to be too low to permit the use of specific gravity determinations for reliable estimations of total proteins in plasma. Cook, Keay and McIntosh (1945) state about these two methods that "Collectively the agreement is fairly good but individually the agreement is far from perfect". Cantarow and Max Trumper (1945) mention that the specific gravity method of determining plasma proteins have been found to be very useful clinically but may give erroneous results under certain conditions. Cole, Allison and Boyden (1943) found that the linear relationship between protein concentration and specific gravity of normal rabbit plasma does not hold good for rabbits in a state of shock.

The Method—In the present series of experiments, Phillips et al method was used for finding specific gravities of plasma and micro-Kjeldahl method was used for determining nitrogen from the serum. The total proteins obtained by the use of these methods were then compared with each other. In spite of the conflicting opinions regarding the reliability of the results obtained by specific gravity method, the present investigations were undertaken to test

the extent of utility of the method of Phillips et al (1944) which is extremely simple and quicker than the micro-Kjeldahl method

Serum was used in all these investigations for finding specific gravities and for determining nitrogen by the micro-Kjeldahl method. These figures were converted into plasma proteins by applying the necessary correction as mentioned in the method by Phillips et al (1944). Blood was collected in clean, dry, plain test tubes from subjects, taking care to see that the tourniquets were not applied for more than one minute at a time. The blood was allowed to coagulate and serum was separated by centrifuging the sample. The serum so separated was used for both the methods.

A stock solution of copper sulphate of 1.100 specific gravity was prepared by shaking finely powdered copper sulphate with distilled water. Copper sulphate solutions of various gravities ranging from 1.015 to 1.075 were prepared by appropriate dilutions of this stock solution. The specific gravities of these solutions were tested with standard hydrometers. The serum was taken in a pipette and drops were delivered from a height of one centimeter from the upper surface of the solutions. The specific gravity of the solution wherein the drop remained stationary for sometime after losing its momentum was considered the specific gravity of serum.

The total plasma proteins were calculated from the formula used by Phillips et al (1944). The formula is given below—Total plasma proteins = 343 (Specific Gravity of plasma - 1.007)

In 1945 Phillips et al put forth two separate formulae for finding total proteins from the specific gravity of serum. One for sera from normal subjects and another for sera in pathological conditions. Hoch and Marrack (1945) working on pregnant women before and after delivery did not find the formulae suitable. As the applicability of the revised formulae of Phillips et al for different diseases is still not verified the original formula was used in this work. Use of the original formula, with the technic of carrying out micro-Kjeldahl estimates employed in this laboratory, appeared to give more concordant results.

The following technique was used for the micro-Kjeldahl method. Serum was kept at 37°C for half an hour. It was diluted to 50 volumes with normal saline. One ccm of the diluted serum was mixed with one ccm of acid digestion mixture. The whole was heated on a micro-burner till the mixture was charred. A few drops of hydrogen peroxide were added to the charred mixture. The mixture was heated till the colour changed to pale straw colour. The mixture was then diluted with water, nesslerised and compared for the intensity of the colour in a Klett-Sommerson photo-electric colorimeter. A standard blank was prepared for each estimation. The non-protein nitrogen was estimated by Folin and Wu's method (1934). Necessary correction was applied for the quantity of nitrogen introduced by addition of hydrogen peroxide. The percentage of total proteins was calculated by the usual formula.

The falling drop method of Phillips et al (1944) did not require any temperature corrections as the room temperatures remained between 28°C to 32°C for all the tests. During the work it was noticed that a layer of thin scum was formed on the surface of the copper sulphate solutions. The serum at times interfered with the falling of drops and it was necessary to break it by gentle shaking about half an hour before the test was started. During shaking it was necessary to see that the settled drops were not disturbed. The serum was tested for specific gravity immediately it was separated from the blood to avoid evaporation.

Table No 1

Results as obtained by Specific gravity method of Phillips and his associates and by Micro Kjeldahl method

a = gms total plasma proteins by the Specific gravity method per 100 c.cms

b = gms total plasma proteins by the Micro-Kjeldahl method per 100 c.cms

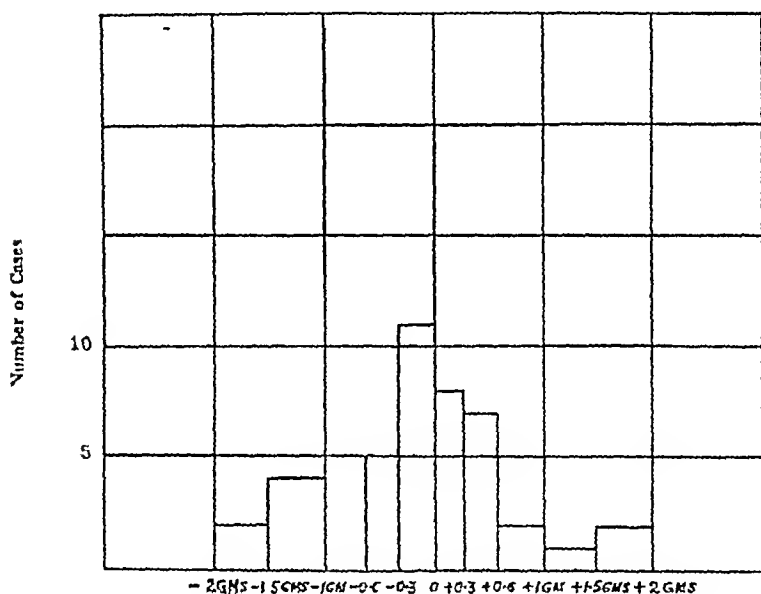
Normal Cases				Acute Nephritis			
No	a	b	a-b				
1	0.09	0.85	-0.10	35	5.48	5.72	-0.24
2	0.35	7.02	-0.07	36	8.23	8.75	-0.52
3	7.03	0.96	+0.07				
4	0.35	0.06	-0.31				
5	7.72	7.52	+0.2	37	0.52	0.68	-0.16
6	7.03	7.91	-0.88	38	0.15	5.92	+0.43
7	7.37	7.59	-0.22				
Oedema Cases				Enlarged Prostate			
No	a	b	a-b				
8	7.54	5.08	+1.86				
9	3.77	4.89	-1.12				
10	4.80	4.07	+0.17	39	0.08	7.72	-1.01
11	0.86	7.0	-1.04				
12	0.48	0.02	+0.40				
13	4.8	1.47	+0.33	40	0.86	0.48	+0.38
14	7.72	7.53	+0.19				
15	4.63	5.05	-1.02				
16	3.0	4.12	-0.52				
17	4.63	4.81	-0.18	41	7.77	7.2	+0.17
18	3.06	4.28	-0.68				
19	4.29	4.07	-0.38				
20	3.26	3.00	-0.71	42	7.03	0.6	+0.43
21	0.17	8.12	-1.95				
22	7.03	5.24	+1.07				
23	5.06	0.47	-0.8	43	7.03	7.06	-0.03
Retention of Urine				Pyonephrosis			
No	a	b	a-b				
24	0.15	0.15	0.74				
25	0.31	6.30	-0.05	44	7.72	7.75	-0.03
26	7.03	7.17	-0.14				
27	7.37	0.03	+1.32	45	8.05	7.2	+0.85
28	8.75	10.5	-1.75				
Hypertension				Persistent Hiccough			
No	a	b	a-b				
29	4.45	4.06	+0.39				
30	7.72	7.36	+0.36	46	4.63	4.78	-0.15
31	8.23	7.5	+0.73				
32	0.17	0.1	+0.27	47	5.90	0.21	-0.31
33	7.03	0.81	+0.22				
34	0.86	0.84	+0.02				
				Pancreatic Calculi			
No	a	b	a-b				
				43	7.03	7.06	-0.03
				Procedentia			
No	a	b	a-b				
				44	7.72	7.75	-0.03
				T B Spine.			
No	a	b	a-b				
				45	8.05	7.2	+0.85
				Severe Anaemia			
No	a	b	a-b				
				46	4.63	4.78	-0.15
				Rat Bite			
No	a	b	a-b				
				47	5.90	0.21	-0.31

The Material—Samples of blood were collected from 40 patients undergoing treatment for the diseases shown in Table No 2 from the King Edward VII Memorial Hospital Bombay, and also from 7 cases of apparently normal and healthy persons from the staff of Seth Gordhandas Sunderdas Medical College, Bombay.

The Results—Total plasma proteins as obtained by the two methods along with their differences are shown in table No 1.

Discussion—The 47 cases that were studied could be classed in three groups Group I which shows an error in values of proteins less than ± 0.3 gms per 100 ccm of plasma, as per the claims of Phillips et al (1944) Group II which shows an error less than ± 0.6 gms proteins per 100 ccms plasma (Moor and Slyke, 1930) Group III in which the error is more than ± 0.6 gms proteins per 100 ccms plasma Out of the 47 cases, 19 cases fall in group No 1, 31 cases in group No II and 16 cases in group III Cases lying in group No 1 form 40.4 per cent of the total cases Adams and Ballon (1946) find this percentage at 44 per cent of their total cases

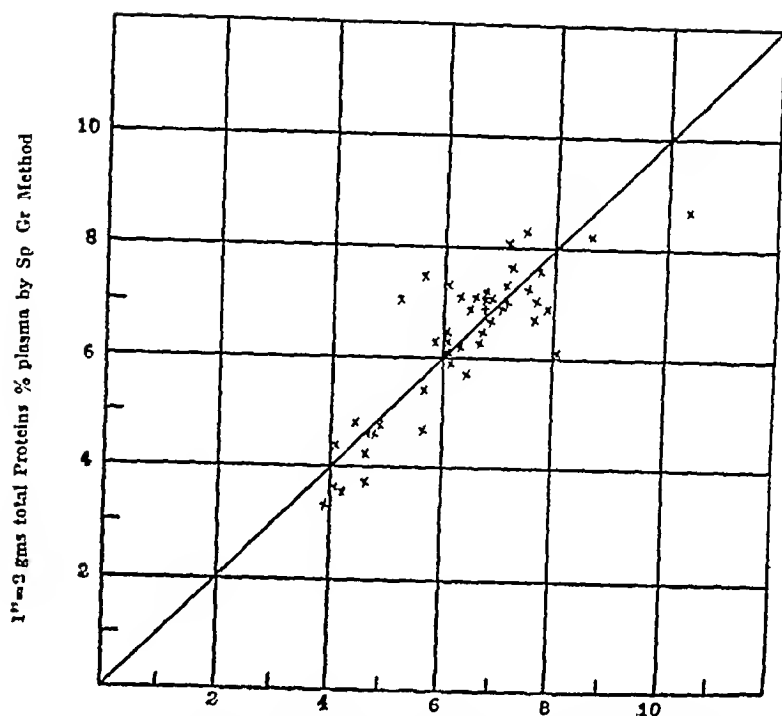
Graph No I shows group deviations of the total plasma proteins by the two methods both on the plus and minus sides



Graph No I —Deviations in values of Proteins in groups between
Specific Gravity Method and Micro-Kjeldahl method

Graph No II shows the total plasma protein figures obtained by the two methods. Markings below the line indicate lower figures obtained by the specific gravity method, when compared with micro-Kjeldahl method

Markings above the line indicate higher figures obtained by the specific gravity method when compared with the micro-Kjeldahl method. It will be seen that the variations lie almost equally on both sides of the line. This was an added reason for the use of the original Moor and Slyke (1930) formula for finding total proteins



Graph No 2 —Proteins by Sp gr method and by Micro-Kjeldahl Method

Clinical conditions of subjects whose investigations were carried out are shown in Table No 2

TABLE No 2
Classification of Clinical Conditions of Subjects

Clinical condition	No. of cases studied	No. of Cases showing agreement with Micro-Kjeldahl method ± 0.6 gms. proteins	No. of Cases showing agreement with Micro-Kjeldahl method upto ± 0.6 gms proteins
1 Normal	7	5	-
2 Oedema			
Acute Nephritis	2	0	2
Subacute Nephritis	2	1	1
Hypertension	2	2	0
Ascitis	3	2	1
Nutritional oedema	2	1	1
Exfoliative dermatitis in Syphilitic patients	3	1	2
Congestive Cardiac failure	2	0	2
8 Retention of Urine	5	3	-
4 Hypertension	6	5	1
3 Acute Nephritis	2	2	0
6 Enlarged Prostate	-	2	0
7 Miscellaneous			
Chronic Nephritis	1	0	1
Bladder calculi with hypertension	1	1	0
Pyonephrosis	1	1	0
Persistent Hiccough	1	1	0
Pancreatic Calculi	1	1	0
Procedentia	1	1	0
Tb Spine	1	0	1
Severe Anaemia	1	1	0
Rat bite	1	1	0
	47	31	16

Out of the 7 normal subjects, 2 showed variations exceeding ± 0.6 gms proteins per 100 ccms plasma. On further investigations it was found that one of these though apparently healthy had donated blood a number of times and the second though apparently healthy had a blood sedimentation rate of 15 mms at the end of 60 minutes by the Westergren technique. From these clinical conditions, no one particular cause can be made out for the variations that are got by the two methods.

SUMMARY

- 1 Forty-seven cases were studied for determining the total plasma proteins by the specific gravity method of Phillips et al.
- 2 Thirty-one cases showed results lying within the limit of ± 0.6 gms proteins per 100 ccms of plasma when compared with the micro-Kjeldahl method.
- 3 The methods of Phillips et al (1944) as it exists today requires some modifications and is still not sufficiently reliable for use in a general hospital as a substitute for finding total proteins by the micro-Kjeldahl method.

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CONCERNING PRESCRIPTIONS

THOMAS DRAPER,

VELLORE

What I propose to say to you here is of a two-fold nature. My subject will consist for the most part of protest and proposal, of lament and laudable aspiration. To me this seems an opportune moment for the frank discussion of certain tendencies which in my opinion are derogatory to our profession. I submit that in respect of the matter to which my subject is limited we are on a slippery slope leading to rapid decline and eventual extinction. I think we must admit that the average Indian physician is a very poor prescriber. Either he sticks to the hospital pharmacopoeia or he falls back upon the manufactured proprietary medicine. In the first case forgetting that every patient is a separate clinical entity needing to be determined on its own merits, and that the routine use of set prescriptions is a practice which is now relegated to the past, or in the latter case that he has ceased to think for himself and has become a mere automaton, handing on prescriptions of which, oftentimes, he does not possess even an elementary knowledge. In the last (7th) annual conference of the All India Pharmaceutical Association, certain resolutions were moved. One was to the effect that a stop should be put to the extravagant and often ill-supported claims made by parties manufacturing or distributing proprietary medicines. A second resolution deplored the multiplicity of names often attached to a single substance and asked for legislation to control this abuse. To pass resolutions in an easy matter, to get them carried out is where the difficulty lies. For this desirable end the closest co-operation is needed between the twin sciences of medicine and pharmacy. How can we contribute to this laudable end? Possibly we may divide our readers into three broad classes.

First those of the extreme left. The "Therapeutic Nihilists" they may be called. The followers of Osler, who at the beginning of this century had largely scrapped the use of drugs. They put all their energies into diagnosis, leaving treatment to nature, good-feeding and nursing.

Secondly those of the extreme right. The full-blown empiricist. The prescriber who falls back upon tradition, usage and experience. For my own part I knew a doctor not more than five years back whose habit it was to write in an ordinary expectorant mixture from 10 to 15 different drugs. I said 'ordinary' but undoubtedly the final combination would be extraordinary. Nevertheless the long array of medicines impressed the patient and this physician had one of the largest practices in the city of Karachi. It may be that some of us here are guilty of this polyglot prescribing, not perhaps writing such, but employing proprietaries of such a nature. Such preparations are not hard to find. Tinctura Antiperiodica, Warburg's Tincture, B.P.C., has no fewer than nineteen ingredients.

Lastly there are those who are always on tip-toes for the latest treatment. This would on the surface seem to be altogether an

admirable attitude to take What have we against such? First of all, the risk involved Secondly, the expense entailed Thirdly, their implicit faith in the manufacturers of the drug Fourthly, failure to appreciate the danger of raising in the patient a tolerance which will afterwards make the drug of little value in a real crisis Lastly, the loss of all sense of proportion which in the event of failure of the drug or idiosyncrasy on the part of the patient, leaves them at a loss as to what to do They have only the one plank by which to cross the stream, that failing no bridge is left to them

Let me enlarge upon these points "The risk involved"

An outstanding example of this was the American tragedy in the use of sulphanilamide Not being a water soluble drug a firm of chemists manufactured an elixir, using as a solvent diethylene glycol 73 people died from this preparation before its danger was discovered In this connection it should be remembered that toxic manifestations do not always immediately occur Ehrlich who coined his first organic arsenical the name "atoxyl" was responsible for many cases of optic atrophy and blindness before it was discovered that "atoxyl" was highly toxic in this way Coming down to the present day you may have been interested in an article in the December 1946 number of *The Indian Physician*—"Two sudden deaths in the V J Hospital, Amritsar due to Neptal" A man and a woman both of middle age, to each were given 2 c c of Neptal diluted in 10 c c of 25 per cent Glucose, intravenously The one died in 2 minutes, and the other in 4 minutes after the injection which was administered slowly and free from technical error Coming to Vellore we have recently had a patient taking Pethidine Hydrochloride as a Morphine substitute This patient wrote to us for another 100 ampoules, having taken home with him when leaving here 100 ampoules of the drug On January 2nd of this year I enquired as to his condition only to learn that he was delirious and that his family had been sent for Knowing that Pethidine in some cases is an excitant having a "cocktail effect" I was not surprised to learn of these manifestations Before commencing Pethidine he had used Morphine for the relief of pain Would he not have been wiser to have continued with this latter drug?

"The costly nature of so many of the newer drugs" This may appear to some of you to be of so mundane a character as to be unworthy of any discussion Money, however, has to be found and in an institution such as ours where we are spending the money of others who oftentimes have donated it at great personal sacrifice, we ought to weigh well this matter of cost I am not suggesting that on the ground of expense we should withhold any life saving measures, but I want to impress upon you that proprietary medicines are naturally bought at much higher rates than their true value I always remember the report issued by a New York hospital management They ordered that in all cases the proprietary medicine should be substituted by the corresponding official drug By so doing they saved over Rs 15,000 monthly on their drug outlay Take the example of a simple substance such as Procainae Hydrochloridum, B.P It costs about one

quarter as much as the proprietary substance Novocaine. Or the B P substance Aneurine Hydrochloride 3 mgm tablets cost about 30 sh per thousand, Berin costs about 3 times more. Put side by side the relative costs of Agotan (Howard) and the B P Cincophenum, or Cardiazolum (Knoll) with its B P equivalent Lepiazolum. The trouble is many firms are not interested in selling to us the B P drugs, they much prefer to draw the extra profits and to be free from danger which they run whenever a B P standard is accepted but not maintained. We have recently seen in the literature the good results obtained by Folic acid in macrocytic anaemias. The present cost of Folic acid tablet is Rs 18 per 25 tablets. A few days ago literature on (Livozyme) a popular proprietary medicine reached me. The makers of this, a firm of exiled chemists from Europe, now in India, have suddenly discovered that this preparation is rich in Folic Acid. Very likely it is, but no one would have known it had not Folic Acid been isolated. 'Cum grano salis' (with a grain of salt) is a motto I advise you to adopt towards many of these pamphlets.

"The implicit faith many of the profession have in all things new" I suppose I am guilty of orthodoxy, have ingrained within me a rigid conservatism. So much so that I am not prepared to say that all cases of bacillary dysentery should be given a sulpha drug, often times the old treatment with salines is just as effectual and relapses are not more numerous. It is not necessary to give every case of infection a sulphanamide, nor is it wise to prescribe thiouracil for every case of hyperthyroidism. It is well to call to mind that the efficacy and speed of action of modern drugs is often accompanied by a dangerously narrow margin between the effective and the toxic dose, and this margin is not always exactly measurable in terms of the individual human response. The B P has dropped the formerly official "Acetanilidum" because of the danger of an agranulocytosis, whereas the U.S.P. still retains it. Not always do I put the B P before the U.S.P., but in this case I submit one is justified in so doing.

"The tolerance often established which will later on make the drug of no effect." This was forcibly brought home to me by a regrettable experience I had with a patient in England. A middle-aged robust farmer developed middle ear trouble and a commencing mastoid abscess. I put him on to sulphonamides, his temperature came down, his pain ceased and apart from a slight discharge from the ear he was apparently cured. A month or so later his symptoms returned more acutely, therefore, I sent him to the E N T Specialist in Addenbrook's Hospital Cambridge. Some days after so doing I was rung up by this specialist asking me "Had I given this patient Sulphonamide?" "Yes" "How much?" "Well, he does not respond now." Finally a temporo-sphenoidal abscess developed, meningitis followed drainage and the patient died. Indirectly I caused his death, and in so doing learned an important lesson, viz, that small doses of sulphanomides are fraught with future danger, and that only in grave conditions and as a life saving measure should sulphanomides be given at all.

'Loss of all sense of proportion' We have gone very far from

the days when a London physician was put into prison because his prescription did not conform to the pharmacopoeia of Galenus That was the 16th century but have we not swung to the other extreme and allowed ourselves to be imprisoned in our thinking in terms of proprietary medicines and perhaps a dozen or so of the latest therapeutic cure-alls? To remedy these existing abuses and dangers, what can be done?

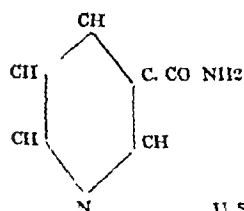
First of all, we must seek the aid of governmental restrictive legislation

Secondly, we must hasten the formulating of an official Indian Pharmacopoeia

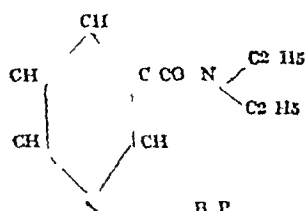
Thirdly, we need to acquire a wider knowledge of the whole field of drug therapy

Fourthly, we must refuse to prescribe any drug that is not supported by official standards or extensive pharmacological experimentation and clinical trial

"Restrictive legislation" This is of the first importance So long as firms are able to make, without let or hindrance, the widest claims for their particular preparations so long must we endure the multiplicity of medicines, often under coined names, about which we know nothing at all apart from what the interested parties have to tell us Take for example the synthetical preparation Coramine, Nicamide, Cycliton, Anacardone or whatever other name has been given to it This drug at long last has found its way into the B P as Nikethamide and into the U.S.P as Nicotinamide, Nicotinic Acid Amide or Niacinamide The U.S.P preparation is the true amide of pyridine—B Carboxylic acid, the B P is the di-ethyl derivative of this



U S P



B P

That is it is not Nicotinamide but Nicotinic acid diethylamide How many doctors know anything about this drug apart from what the makers (Messrs Ciba Ltd) have told them? This is what Thienes writes about it—

"Nikethamide is extensively used, often without sufficient cause in the treatment of acute respiratory or circulatory failure due either to drugs or to infection There is neither adequate experimental basis nor carefully controlled clinical study to support the popularity which this drug enjoys Clinical experience suggests its usefulness in shock, but critical evidence of its value is lacking It is perhaps the drug of choice in morphine poisoning, Maloney and Tatum (1932) state that it is more certain, safe, and enduring than metrazol for this purpose It is inferior to picrotoxin and metrazol in treatment of depression by barbiturates, chloral hydrate, paraldehyde and tribromoethanol" Sollman remarks on it in a similar

way—"They (Leptazolium and Nikethamidum) were introduced as substitutes for camphor, to produce respiratory and circulatory stimulation in collapse, but they have little effect unless their dosage approaches the convulsive. The therapeutic claims tend to go beyond this rather limited field." What is needed in India is an official body charged with the task of investigating such claims, publishing and controlling a list of new remedies, able to prosecute if need be in cases of flagrant fraud and misstatement, a body on the lines of the Council of Pharmacy and Chemistry existing in the U.S.A. who after a drug has been proved useful cause it to be included in their list of New and Non-official Remedies.

The formulating of an Indian Pharmacopoeia under a joint board of chemists, scientists and the medical profession. Such a book issued under the authority of the Government of India—a statutory volume backed by full powers to punish delinquents is more than over-due. This brings me to my second suggestion. The formulating of an All-Indian Pharmacopoeia. Until this is an accomplished fact we are powerless to act. Government cannot pass a pure food and drug act until we know what is meant by the term—a pure drug. One cannot institute proceedings against proprietary medicines because they are what the manufacturer likes to make them. If we take up a 2 c.c. ampoule of any liver extract and read that it equals 1,000 grammes of raw liver we cannot prove or disprove that statement. There is no standard either chemical or biological to which appeal can be made. Supposing the Indian made Chloroform contains impurities which render it highly dangerous as an anaesthetic no prosecution will avail unless there is first of all an official standard and the manufacturer has sold it under a declaration that it is in conformity with that standard. We all are, or we should be, very much alive to this need, a modern Indian Pharmacopoeia. Nothing officially has been attempted since the Government of India in 1900 issued *The Indian and Colonial Addendum to the B. P. 1914*. This standard work contained a number of Indian drugs that were not in the B. P. and also a number of drugs of Indian origin that could be used in the place of the B. P. drug. Of the former such drugs as *Alstonia*, *Abroma*, *Kurchi*, *Isphagula* were made official, of the latter Indian *Valerian*, Indian *Sarpagilla*, Indian *Scilla* and *Myrabolans* instead of *Galls*. These substances were not taken seriously and many of them could not be obtained from wholesale druggists English or Indian. It is not surprising, therefore, that this standard work of reference died out completely. An entirely Indian Pharmacopoeia which will include the B. P. the U.S.P. and indigenous drugs is now overdue.

Thirdly I made the plea that we who practise medicine in India take a comprehensive view of the whole range of therapeutic medicines. It is not generally known that the B. P. has now about 820 monographs on drugs and the U.S.P. a rather smaller number. The reason for the smaller number of the latter is to be found in the fact that it is more recent, and that whilst the U.S.P. XII has added 165 new drugs to those in the U.S.P. XI, it has at the same time removed 120 drugs that were formerly official—*Acriflavina*, *Capsicum*,

Fodophyllum, Santal, substances still in the B.P., and in the U.S.P. XI are no longer official U.S.P. XII preparations. The B.P. has added through its 7 addenda all the modern drugs, but has not been able to delete many of its obsolete preparations. For example, of vegetable bitters the B.P. has Gentian, Quassia, Calumba and Serpentaria. The U.S.P. has one only, viz., Gentian. Another reason why it is most necessary for the Indian physician to acquire a more comprehensive knowledge of his armamentarium is in order that he may assist the pharmacist in his prescribing. If he wishes to prescribe an organic mercury compound as a diuretic let him use one name only, i.e., that of the B.P. or as it will be in due time that of its Indian equivalent—Mersalyum B.P. and not Neptal, Salyrgan or Novurit. If he wishes to use a diuretic of the Xanthine class let him stick to the official names for these substances. Aminophylline is not official nor is Cardophyllin or even Diuretin. The B.P. name is Theophylline cum Ethylene Diamine. It is regrettable that the B.P. and the U.S.P. have added to the general confusion by the use of different nomenclature. This seems to be a case of sheer perversity such as when the B.P. calls Cardiazolum, Leptazolum, and the U.S.P. calls it Metrazolum. Or when the U.S.P. takes Atebrin and calls it Quinacrine and the B.P. calls it Mepacrine. It is surprising how many U.S.P. names take as a synonym the B.P. name and vice versa. The U.S.P. has Aethylis Carbamas. Synonym Urethane. The B.P. has Urethane and the synonym Ethyl Carbamate. Even in a simple substance such as Resin the B.P. has Colophony, Syn. Resina. The U.S.P. has Resina, Synonym—Colophony, one is left wondering. The whole thing is absurd, and still worse, in a country where both pharmacopoeias are in use, highly confusing. Recently there has been a revival in the use of Dolantin. A pre-war German proprietary that was taken up and adopted in the U.S. as Demerol and later in Britain as Pethidine. Dolantin, Demerol, Pethidine, why not prescribe these as Methyl-Phenyl-piperidine carboxylic acid and leave the coined names to the pharmacist? Put yourself in the place of the dispenser. Not so long ago I ordered Cincophenum B.P. The dispenser had never previously heard the name but she was familiar with the same drug under its proprietary names Agotan and Atophan. The same may be said of Chiniofonum, Phemitonum, Thio-pentone, Hexabarbitonum, Pento-barbitonum, Amylocaine, Procaine and many others. What are the official names for Caprokol, Carbarsone, Cardiazol and Carbromal? It does seem strange that many a doctor who orders these drugs does not know what they are! This brings me to my last suggestion, viz., do not prescribe any drug until you know at least its composition, therapeutic index, and toxic effects. There is a story related by Gee in his Aphorisms which is well to the point. "Some years ago a gentleman brought his daughter to see me on account of enlarged glands in the neck. Whilst I was prescribing the treatment he suddenly asked me what was the use of the said glands? I at once called to mind the story they tell of Razes, who became blind in his old age. At first he thought of having his eyes operated upon, and he consulted a surgeon for that purpose. But

EMERGENCY MANAGEMENT

ITS ADMINISTRATIVE ASPECTS

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In August 1942 we had our first experience of a sudden emergency when 159 casualties were brought to the Hospital in the course of three days out of which 74 were admitted and 85 were treated in the Casualty and sent home. At that time we were totally unprepared to deal with the situation. The experience gained on that occasion and the shortcomings that were observed made us conscious about the necessity of improvising a plan to meet such emergencies efficiently. In January 1943 A.R.P. measures were improvised for the safety of the hospital patients and staff, and a plan to meet any sudden influx of casualties was also chalked out. This plan was rather complicated, as we had not only to provide for a sudden onrush of casualties, but also to organise fire fighting squads, rescue parties, demobilisation squads, fire watchers on the roof tops, to erect blast walls and organise shelters. The second emergency was experienced on 14th April 1944 when 211 casualties were brought to the hospital during the course of 4 hours out of which 92 were admitted. The real test of our organisation however, was in the recent R I N firing when 314 cases were brought to the hospital out of which 208 were admitted as inpatients in the course of 7 hours.

Let me first state the difficulties and shortcomings experienced in the past emergencies. They were —

Lack of discipline in student volunteers — To cope with the sudden rush of patients, student volunteers were called to the out-patient department for help. They responded magnificently and were keen to render assistance, but they did not know what was expected of them. There were junior students who were not acquainted with hospital routine at all. They left the cases allotted to them and went to see something that was more interesting, they crowded round in the out-patient or stood in groups at the entrance of the department to watch the casualties being brought in, and created an impression of disorder and panic. Their disorderly work was actually a source of hindrance than help.

Incomplete Registration — Difficulty was experienced in the proper registration of names, addresses and other particulars of patients with the result that relatives of serious patients dying shortly after admission could not be communicated with. This work of registration was entrusted to the students. Not being acquainted with this nature of work, they omitted several important details, which could have been easily obtained from the patient while he was alive or from those who brought him to the hospital.

A Paper read at the 64th Meeting of the G. S. Medical College and K. E. M. Hospital Staff Society held on October 12th 1946 with Dr R. N. Cooper in the Chair.

Waste of time and moving round a patient from department to department—It was noticed that the usual routine of dealing with the casualties in the out-patient department was very slow and could not effectively cope up with the rush of work. In normal times before a casualty is sent to the ward, his name, address, locality where injured, his injuries and such other details are taken down by the casualty officer in the casualty register. He is given a prophylactic dose of anti-tetanic serum, then he is taken to the registration office where his case papers are prepared, and all the details mentioned above are again entered in the out-patient register. All this takes a considerable time and the patient has to be moved from one department to another. During the R.I.N. disturbance the casualties were brought in at the rate of one every minute; they had to wait on stretchers in the O.P.D. hall before the details mentioned above were attended to. Such a spectacle of patients lying in agony created a bad psychological impression.

Minor Casualties—A large number of minor casualties only needing dressing had to be disposed off by the casualty officers. The two tables and the staff in the casualty department were quite inadequate to deal quickly with the large number of casualties. The labour staff in the out-patient department was also quite inadequate to cope with the sudden rush and particularly to carry the stretchers to the wards.

Patients' Valuables—It was noticed that when a patient was taken in the ward, the labour staff removed his clothes and came in contact with his valuables. This was not very desirable.

Insufficient Staff—In the wards of the usual number of nursing staff could not attend to the sudden increase of work. The house surgeon being constantly busy in the operation theatre, there was no one to prepare the cases for operation and to write their histories.

Confusion in wards and theatres—Several wards were started for the reception of casualties at the same time with the result that several members of the Honorary Staff were called as soon as the emergency started. This led to much confusion in the operation theatre, patients belonging to one Honorary Surgeon were operated upon by another. Later, the surgeon who operated, lost sight of the case and the surgeon under whose care the patient was admitted was not quite conversant with the details of the operation.

Lack of proper resuscitation—Another drawback was lack of properly organised resuscitation and whatever effort that was made was not methodical. This important detail was left to the medical registrars alone. Very often cases were rushed to the theatres without any resuscitation and a queue of trolleys could be seen outside the operation theatres, the patients were waiting for their turn of operation for quite a long time, sometimes without any attendant by their side. The result naturally was, unnecessary suffering to the patients and a high percentage of mortality.

Delay in transfusions and obtaining material from stores—Considerable difficulty was felt, particularly as regards administration of salines, plasma and blood, firstly because these materials had to be indented in each individual case then the ward boy had to run

to the office to obtain the sanction and then to the Clinical Pathology department to obtain the material and then back again to the ward. Several times ward boys were seen running along the corridors of the hospital chasing the administrative officers to obtain their sanction. This running about added to the confusion, and the labour staff which was badly needed in the emergency ward, was not available. Secondly, enough transfusion apparatus were not in readiness in the wards, considerable time was needed to clean and sterilise them each time. Similar difficulty was experienced by the ward sisters in obtaining injections and other materials from the medical, general, diet and linen stores.

Difficulties in the disposal of the dead—During the R.I.N. disturbances, not a single relative turned up to claim a dead body during the first three days. On the fourth day only three bodies were claimed and removed and on the fifth day nine bodies. The cold room was packed ceiling high with dead bodies, the dead bodies had to be taken out every day and kept out in the open for identification. The cold room had to be opened very often, and its temperature could not be maintained, with the result that decomposition was going on in full swing. It was on the 6th day of the disturbance that the relief organisations came to life and removed 50 bodies, in a state of advanced decomposition, when they were unrecognizable. Later many relatives and friends turned up to make enquiries. But there was no means of identifying the unknown bodies which had undergone putrefaction or those that were disposed of by the relief organisations.

There were quite a number of unknown among the dead, and it was difficult to decide from the indoor case papers as to which particular body the paper referred to.

Being aware of the situation in the city and the likelihood of disturbances on a large scale, the Dean convened a Conference of the Administrative Staff, to discuss the difficulties experienced in the past emergencies or those that were likely to arise and to evolve a suitable plan.

Plan for Emergency—It has been decided that in case more than 5 casualties arising out of such disturbances are received within 15 minutes, the casualty officer should immediately inform the Dean, who would consider the situation and declare a state of emergency, when the usual routine would be abandoned and a quicker method of dealing with the casualties adopted. The salient feature of the plan would be as follows—

Signal to declare a state of emergency—The bells near the X-ray Department and the R.M.O.s' quarters would be rung continuously for two minutes to announce a state of emergency in the hospital. On hearing this signal each individual member on the staff of this hospital and the students shall take up their post of duty as mentioned at the end of this paper—and start working immediately.

Organised student volunteers—The Dean and the A.M.O. (Jr) will be in the out-patient department supervising the reception and distribution of casualties. The Dean will go round from time to

time visiting the emergency wards and theatres. The hostel superintendent shall collect student volunteers and bring them to the out-patient department. He shall divide them into two batches. A batch of junior students who are not acquainted with the hospital routine and a batch of senior students, particularly those that have done surgical work. These two batches will sit on benches one on each side of the casualty department in the O.P.D. hall in an orderly manner and work under the guidance of the hostel superintendent. The junior students will help in carrying stretchers whenever necessary. One senior student will be detailed to be in charge of each casualty admitted as inpatient.

Distribution of casualties—As soon as a casualty is brought in, it will be given a prophylactic dose of anti-tetanic serum and an injection of morphia (if decided by the A.M.O. (Jr.)). The injections will be given by a nurse who will be present in the O.P.D. hall with the necessary equipment on a trolley. Then the A.M.O. (Jr.) and the senior casualty officer will decide whether it needs admission or can be treated in the casualty room and sent home, and direct it accordingly. A patient needing casualty treatment only, will be made to sit on a bench in proper order. One who needs indoor admission will be referred to the head clerk (registration).

Disc System Prompt admission and care of casualties—The head clerk (registration) will be present in the O.P.D. hall. In those cases which have been referred to him by A.M.O. (Jr.) for admission he will take down the name of the patient, the name of the person who brought him to the hospital and the locality where he was injured. He will also write the name of the student to whom the case is allotted and enter the disc number against his name—a disc system has been devised to avoid moving of the casualty from one department to another and to minimise the time needed for entering the details of registration. According to this system a cardboard disc bearing the serial number is tied round the patient's neck and another disc with identical number is tied round the arm of the student in charge so that the student to whom the case was allotted can be easily traced from the list maintained by the head clerk (registration). A blank O.P.D. and indoor paper is then handed to the student. The patient is then straight away carried to the ward accompanied by the student in charge. By this method a casualty needing admission will not remain in the out-patient for more than 5 minutes. From this time onwards the student, as it were, becomes the guardian-angel of the patient. He will write the history of the case, prepare the patient for operation and carry out any other orders given by the house surgeon, medical registrar or the Assistant Honorary Physician. He will accompany the patient to the operation theatre and write down the details of operation on the indoor case paper as dictated by the surgeon during the course of the operation. He will not leave the patient till he is out of anaesthesia, or out of danger or dies, and then too, only under the instructions of the house surgeon. The same student will follow up the case from day to day, do his dressing and write the daily case notes. This is ex-

pected to ensure proper care of the patient and maintenance of case notes

Safety of patients' valuables and details of registration—In the ward, the valuables will be removed from the patient in the presence of the sister and the cash clerk from the office, who will be present in the emergency ward from the time the state of emergency is declared till it is called off. The valuables will be taken in charge of by the cash clerk, who will enter the details on the spot in his register and prepare a receipt and hand over the same to the sister-in-charge of the ward. Two clerks from the registration section will be on duty in the emergency ward to take down the name, address and other particulars of the patient. They will fill in the O.P.D. and indoor papers and also copy these details in the O.P.D. registers. This will ensure that no important details of registration are missed and the time that was wasted in taking them down in the out-patient is saved. Thus the patient will be carried to the ward within a short time after his arrival into the hospital, and his treatment started immediately.

Emergency ward—Evacuation and rotation of emergency—In order to prevent confusion in the ward and to ensure proper resuscitation, it has been decided that as soon as a state of emergency is declared the A.M.O. (Sr) will arrange to have a ward completely evacuated by transferring all the patients from that ward to medical wards. That ward will be named hereafter as the emergency ward. Only 25 casualties will be admitted under the emergency surgeon, after that the emergency will be switched on to his colleague in the same ward. This is designed for smooth working by preventing overcrowding and admixture of ordinary with emergency cases. Only one unit will be called for work at a time. This will prevent confusion in the operation theatres and also the possibility of one surgeon operating upon cases belonging to another surgeon. This will also ensure sufficient interval of rest for the surgical and medical teams that have once finished their emergency work for 25 casualties.

Organised Resuscitation—In the emergency ward, the resuscitation will be carried out systematically by a team consisting of the house surgeon and medical registrar on emergency duty under the guidance of the Assistant Honorary Physician on emergency duty. Experience has shown that resuscitation of casualty cases before operation, results in a larger percentage of recoveries, as would be seen from the report of cases to be submitted by Dr V. P. Mehta. Another team consisting of the Honorary Surgeon, the Assistant Honorary Surgeon and the surgical registrar on emergency duty will be operating assisted by senior students. The Honorary or Assistant Honorary Surgeon will personally examine and decide the question of operation in every case before the case is taken to the theatre.

Automatic supply of transfusion apparatus, plasma and other items—On declaring a "State of Emergency" the storekeeper is required to send two dozen complete transfusion apparatus to the operation theatre for sterilization. The sister-in-charge of theatre will send one dozen sterilized transfusion apparatus to the emergency ward. (In the theatre one dozen transfusion apparatus will

be always kept ready sterilised) The resident pathologist will supply two dozen bottles of dried plasma to the emergency ward The pharmacist will issue to the ward a sufficient stock of injections, salines, sulpha tablets, etc, that would ordinarily be needed under such circumstances All this would be done automatically so that resuscitation and treatment could be started without delay In case the sisters need any more articles, they are empowered to obtain them directly from the resident pathologist, storekeeper or pharmacist without obtaining sanction from the administrative officers, the indents being scrutinised by the sanctioning authorities later This will prevent confusion caused by the labour staff running about, and they will be available for more useful work in the emergency ward

Identification and disposal of the dead —The problem of identification and disposal of the dead has been simplified by photographing the unknown as soon as they are brought to the cold room before decomposition renders them unrecognisable A separate disc system has been introduced to surmount the difficulty of identifying the bodies and has been working satisfactorily To ensure prompt disposal, communications will be instituted at an early date with the relief organizations to speed up the disposal of unclaimed bodies An attempt is also being made to find out methods which will prevent decomposition

It will be evident from the plan of action, that on declaration of a "State of Emergency" the normal hospital routine, which though satisfactory and efficient in normal times, is unable to cope up with the strain of such occasions It is therefore necessary to modify the routine in such a way that without loss of important details of medico-legal nature and registration, etc It should ensure quick distribution of casualties, a systematic evacuation of wards, prompt admission, resuscitation and treatment without creating confusion It is felt that organised plan as outlined above will help in minimising the discomforts to the patients, and in increasing the number of recoveries with a very much smaller percentage of deaths

SUMMARY OF THE EMERGENCY PLAN

On declaration of a State of Emergency the duties assigned to various officers shall be as follows —

The Dean and the A.M.O (Jr) remain in the outpatient department and supervise the reception and distribution of the casualties to the wards The Dean goes round from time to time visiting the emergency wards and operation theatres

A.M.O (Sr) —He shall at once begin the evacuation of a ward for the emergency to be named Emergency ward He renders whatever help that may be necessary in the management of the wards and theatres

The Assistant Dean —He shall detail the Registration and Cash Clerks to the Emergency Ward

He shall send out intimation to the operation theatres to readiness

He shall arrange the distribution of the labour staff in the wards, operation theatres and other departments

He shall arrange to get donors for blood

He shall supervise the disposal of the dead bodies

The Matron—Shall arrange the distribution of the nursing staff to the O P D, emergency ward and the theatres according to the instructions of the Dean

She shall remain in the O P D

The Assistant Matron (Sr)—Shall render help in the emergency ward

The Assistant Matron (Jr)—Shall remain in the Nurses' Home and carry out the instructions of the Matron

All the Storekeepers shall remain in their respective stores and supply materials to the theatres and wards as mentioned before

The Office Superintendent—Shall communicate with the Honorary Staff under instructions from the Dean

He shall supervise the distribution of the clerical staff in consultation with the Assistant Dean

Honorary and Assistant Honorary Surgeons on emergency duty with their Registrars shall operate upon patients admitted under them

House Surgeon on emergency duty—Shall remain in the Emergency ward and look after the pre and post-operative treatment of patients

Assistant Honorary Physician on emergency duty shall remain in the emergency ward with his Registrar and carry out the work of resuscitation

After 25 cases have been admitted under one Surgeon the emergency shall be shifted to the next medico-surgical unit in the same ward and so on by rotation

(Continued from page 94)

when he found that the surgeon could not tell him how many tunics the eye possesses, Razes reconsidered his intention and threw it up." Fortunately for us our patients are not all of them enlightened as was this famous physician, so we go on in the spirit of the gallant 600 immortalised by Tennyson, "Theirs not to reason why, theirs but to do or die gallant 600"!!

Critical Notes and Abstracts

MERCUPURIN USED ORALLY Batterman, DeGraff and Shori (Am Heart Journal, 1946-31-431) report that the oral administration of a mercurial diuretic is not recommended to replace the intravenous preparations which are superior and are more reliable in producing a diuresis. However, many patients can be benefited by the oral use of a mercurial. This investigation was, therefore, undertaken in an effort to answer the following questions: (1) Is the mercurial diuretic in the form administered orally an effective and safe diuretic for relieving the signs and symptoms of congestive heart failure present in the average patient? (2) If the oral preparation is effective, how should it be administered in order to obtain its maximum value?

The oral preparation of Mercupurin was studied in both hospitalized and ambulatory patients. Each oral tablet contained 170 mg of Mercupurin. The parenteral solution, on the other hand, contains 135 mg in 1 cc. A total of 81 patients presenting all stages of congestive heart failure were given Mercupurin orally. Fifty-six were treated exclusively as hospitalized patients, five were observed as both hospitalized and ambulatory patients.

A practical and relatively quick appraisal of the effectiveness of a diuretic can be gained in hospitalized patients by administration of the preparation after preliminary period sufficiently long to evaluate concomitant therapeutic measures, such as bed rest, digitalization, or the effectiveness of other diuretic agents. A diuretic response is considered to be an effective one if the patient loses at least three pounds of edema fluid. In the single dose method, this response should occur within 48 hours. When the multiple dose method is used, the diuresis should occur during the period of administration, or at least no later than 24 hours after the drug is discontinued.

I Single Dose Method—A single dose of five tablets was given to 24 patients for a total of 31 trials. A satisfactory response was obtained in 18 trials (58 per cent), or 16 patients (67 per cent). Diuresis usually began within 4 to 12 hours, and with few exceptions completed in less than 24 hours. This method of administration is not reliable and the degree of diuresis obtained by its use does not approach that produced by the intravenous preparation.

II Multiple Dose Method—One to three tablets three times daily for a period of two to five days constituted a trial or course of treatment. Thirty-nine such courses were given to 29 patients. A satisfactory response was obtained in 25 trials (67 per cent), or 20 patients (69 per cent). Diuresis was usually slow in developing and in many patients did not reach its peak until the drug had been given for 48 hours. Nevertheless, the total diuretic response frequently approached that achieved with an intravenous preparation. This method is not the one of choice when rapid removal of edema fluid is desired. It is, however, the ideal method for patients who do not require emergency measures, for those who should have edema

fluid removed gradually, and for those who cannot be given the diuretic parenterally

In considering the seemingly high percentage of failures in our study, it is pointed out that digitalis or ammonium chloride was deliberately withheld in several trials. Our studies convinced us that digitalis effects, as well as simultaneous administration of ammonium chloride, are desirable when an oral diuretic is used. We believe that unsatisfactory responses occurred only in those patients who had a minimal degree of heart failure or in those whose heart disease was so severe that only a parenteral preparation could have resulted in diuresis. The use of the oral preparation is contraindicated when the response to the previous administration of parental diuretic was unsatisfactory.

The multiple dose method has particular value in the treatment of ambulatory patients. The dose and scheme of administration must be determined for each patient. Once these are established, the patient readily learns the most propitious time for self-administration of the tablets. In 10 to 13 ambulatory patients studied, the response was considered to be satisfactory. Out of 152 trials, only eight resulted in an ineffective response.

Toxicity with the multiple dose method was of little consequence in hospitalized patients. Mild gastro-intestinal irritation of a transient nature was observed in only two of the 29 patients. The ambulatory patient seemed more prone to develop gastro-intestinal irritation, since it was noted in 6 of the 13 patients so treated.

Evidence of kidney irritation was observed in only one of the 42 patients treated by the multiple dose method. This consisted of an increasing albuminuria after nineteen months of therapy. The presence of albuminuria was not, however, considered to contraindicate the continuation of therapy.

III Daily Dose Method—The daily maintenance dose of Mercupurin administered orally was followed in 26 hospitalized patients for 30 trials and in 18 ambulatory patients for 31 trials. All of these patients were in progressively severe congestive heart failure which no longer responded to a maintenance dose of digitalis. With few exceptions all had been receiving frequent injection of Mercupurin intravenously. The 26 hospitalized patients received two tablets in an undivided dose of periods of 7 to 41 days. The ambulatory group of patients have, to date, received from one to two tablets daily for periods of one to 49 weeks. The patients who responded to the daily dose required from 4 to 14 days of continuous therapy before the medication became effective. Of the hospitalized patients an effective diuresis was attained in 73 per cent and of the ambulatory patients in 77 per cent.

The oral administration of Mercupurin failed in seven hospitalized and four ambulatory patients. Failure could be attributed in most cases to the severity of the heart condition. These patients also stopped responding to the intravenous mercurial diuretics. For such patients oral Mercupurin is of no value, and its use may result in mercurialism.

Toxicity associated with the daily dose assumed several forms. The most common untoward reaction was digitalis toxicity related to the phenomena of mobilisation of the digitalis from the edema fluid at the time of diuresis. Of more importance is mercurialism. Gastro-intestinal symptoms associated with increasing albuminuria occurred in three instances. This occurred only in patients who had already presented evidence of kidney disease. All manifestations subsided when the diuretic was discontinued. Four other patients presented increasing albuminuria, but only after continuous therapy for more than thirty weeks. Mild gingivitis was observed in four patients. The gingivitis subsided promptly when therapy was discontinued. The most serious complication was the occurrence of uremia. In two of the hospitalized patients the non-protein nitrogen became elevated. When the medication was discontinued the non-protein nitrogen returned to normal limits, but in the light of this experience, we believe that the oral mercurial should not be used in any patient who presents impaired kidney function, such as fixation of urinary specific gravity.

Comments —The results indicate the value of the maintenance dose of Mercupurin administered orally in the treatment of patients with congestive heart failure. We feel that the effectiveness of the method outweighs the possibility of the occurrence of toxic reactions. It has its greatest usefulness in patients with congestive heart failure who have exhausted the value of maintenance dose of digitalis and who, in spite of repeated injections of a mercurial diuretic, reaccumulate their edema or experience a recurrence of acute symptoms. The oral diuretic will remove all signs and symptoms of failure in such patients, making it possible either to dispense with the intravenous preparation or to decrease the number of injections required.

Book Reviews and Notices

CASE STUDIES IN THE PSYCHOPATHOLOGY OF CRIME Vol Two Cases 6 to 9
By Ben Karpman M D Published by Medical Science Press, Station L Washington,
D C 1946 pp viii and 738 Price \$ 16

This second volume of Case Studies in the Psychopathology of Crime by Ben Karpman, senior medical officer and psychotherapist of St Elizabeth Hospital, Washington, records four case histories in detail. We have not seen the first volume which recorded five case studies and observations thereon in a separate volume named "The Individual Criminal". In that volume the cases studied were individuals charged, in the main, with predatory crimes, the present volume deals with cases directly involving sexual crimes. The author proposes to follow this up by a third volume confined exclusively to murder cases. The cases studied here are of individuals undergoing detention for (1) Theft of US Mail, (2) Drug Addiction, (3) Violation of the Mann Act, White Slavery, (4) Rape, and (5) Mail Train Robbery. The method followed is that of psychoanalysis and there is a considerable amount of dream material presented in each case. The case histories are exciting autobiographies written by four criminals, preceded by a short summary of official records of each case, results of physical examination and a discussion of the data. The author calls these studies "a reference source for research in criminal material", and so he gives one case (case VIII) in the original form as it was analysed, session by session, so that the reader can judge for himself how the material was coming out and how the treatment progressed.

These voluminous studies, we have no doubt, will interest all psychologists, psychiatrists, lawyers, social workers and law makers. They are meant for such mature adults and the sale of the book is limited to those having a direct professional interest in medico-legal and social problems. All students of human nature will learn and understand much from these exhaustive case studies, and will be grateful to the painstaking author. Altogether a valuable contribution to sexual psychopathology and criminology!

CORRECTIONS —

Please make the following corrections in the article on Quinidine in the Treatment of auricular Fibrillation by T K Raman and P Ramkrishna Mudaliar, "Indian Physician", V 6, pp 55-69, March, 1947

(1) Plate II Fig 12 Instead of "Case 7, Leads I II and III" read case 7 Leads I II and II"

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Original Contributions

ON HEADACHE

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Headache is one of the commonest kinds of pain met with in practice. There is hardly a person who has not suffered from headache at some time of life and in some form or other. Yet, our knowledge about its pathogenesis, the physiological mechanism involved in its production, its frequency of occurrence, and its clinical features is still meagre. Recent observations, experimental, surgical and clinical, chiefly of Pickering, and of Wolff, have thrown much light on the mechanism of headache and a brief review of this work will not be out of place. Headache may be defined as pain or discomfort in the head, felt locally or referred distally as a result of extracranial or intracranial disease. Local tenderness of the scalp serves as an index to the structures responsible when pain-sensitive structures are directly irritated. Headache from deep sinuses is referred along the first and second branches of the trigeminal nerve, from the eye it is referred along the first branch of the trigeminal. Headache from intracranial diseases is usually referred pain. Pain referred to the head from disease of tissue elsewhere than the head does not occur, with the rare exception of pain in jaw or neck with angina pectoris.

For convenience, pain in the head may be grouped as under

- (1) Pain arising in the structures of the scalp and neck,
- (2) Pain from the eye,
- (3) Pain from the nasal and the paranasal structures,
- (4) Pain from the disorders of the nerves of the scalp and face neuritis,
- (5) Pain from the nerve ganglia, tic douloureux, hypoglossal and occipital neuralgias,
- (6) Histamine Headache or Horton's Syndrome,
- (7) Headache of Migraine or Hemicrania,
- (8) Headache in Arterial Hypertension,
- (9) Headache associated with changes in intracranial pressure
Brain Tumour Headache, and
- (10) Psychalgia

PAIN SENSITIVE STRUCTURES OF THE HEAD

All structures in the head—tissues covering the cranium and the intracranial structures—are not equally sensitive to pain. The pain sensitive and insensitive structures may be grouped as follows —

Pain Sensitive

- tissues covering the cranium, especially the arteries,
- periosteum,
- intracranial venous sinuses, and their tributaries,
- dura at the base, and that covering the tentorium,
- dural arteries, especially basal,
- V, IV, V cranial nerves,
- cervical 1, 2, 3 nerves

Insensitive

- cranium,
- diploic and emissary veins,
- most of the dura, falx,
- pia arachnoid,
- ependymal lining of the ventricles,
- choroid plexus,
- brain substance

From this it will be seen that the pain sensitive structures are mainly extracranial, and of the intracranial structures, with the exception of the arteries and the sensory nerve trunks, *all the pain sensitive structures are those which anchor the brain to the cranium*. Traction, displacement, distension and inflammation of these intracranial vascular structures are chiefly responsible for headache occurring in intracranial diseases.

Little need be said here about the pain or headache due to *local inflammatory acute or chronic causes*, such as skin or hair follicle infections, abscess, carbuncle, fibrositis, myositis, myalgia, peritosteltis, etc. Inflammation and engorgement of the *nasal and paranasal sinuses* causes pain which has special characters, is easy to recognize and is relieved by aspirin or codeine, and by shrinking or local anaesthetization of the nasal structures. *Pain from the eye* or ocular headache is associated with errors of refraction (except myopia), muscular imbalance, and glaucoma. It is localized in the eyeball or orbit and at worst referred along the first branch of the trigeminal nerve, and sometimes to the occiput and back of the head. Photophobia may be present whenever there is severe headache, or any inflammation of the iris and the ciliary body, or even with normal irides, in the presence of conjunctival irritation. *Pain in neuritis or neuralgia* has special characteristics and gives little difficulty in diagnosis. *Contractions of the muscles of the scalp and neck* are responsible for various sensations described as weight, pressure, cramp, tight band aching, soreness, stiffness, etc. There is tenderness throughout the trapezius muscles along the top of shoulders, and in the upper neck. There is also pain or feeling of pressure over the vertex of the head. Noxious stimuli, or emotional disturbances or circumstances of fatigue, stress or occupation are responsible for this sustained muscular tension, secondarily giving rise to pain from the shoulders neck and head.

The true headache i.e., headache from intracranial structures may be considered in detail

EXPERIMENTAL HEADACHE

Headache can experimentally be produced by (1) injection of histamine and (2) by withdrawing of 20 ml of cerebrospinal fluid

Histamine headache—The intravenous injection of 0.1 mg histamine causes typical headache, which begins one minute after the injection, in half a minute reaches its maximum intensity, and then gradually disappears. It is *throbbing* in character and *generalised* in distribution. Histamine injection causes vasodilation, with flushing of the face, fall in blood pressure, and a rise in skin temperature. The intracranial vessels, meningeal and those on the brain surface, are also dilated and there is an increase in the intracranial pressure. But these—fall in blood pressure and rise in CSF pressure—are not responsible for histamine headache, because the fall in blood pressure and rise in CSF pressure last only for a minute, and the headache begins and reaches its maximal intensity when the blood pressure and CSF pressure are returning or have returned to normal. Again, histamine headache can be relieved by increasing the CSF pressure by compressing both the jugulars or by the intrathecal injection of the normal saline. Histamine headache can also be temporarily relieved by a second injection of histamine or by the inhalation of amyl nitrite, the relief being coincident with the fall in blood pressure. Thus, *the histamine headache is caused by the undue stretching of the arterial wall*, its intensity corresponds with the amplitude of vascular pulsation and it can be relieved by increasing the pressure outside the walls of the intracranial arteries or by diminishing the pressure within them. Febrile headache is akin to histamine headache and can be relieved by intrathecal injection of normal saline.

Drainage headache—Withdrawal of 20 ml of cerebrospinal fluid regularly produces headache in normal erect persons. This headache is relieved by intrathecal injection of normal saline restoring the cerebrospinal fluid volume, by horizontal posture or by head flexion or extension. Drainage headache is independent of estimated intracranial pressure. It is caused by traction by the brain upon the pain-sensitive structures which anchor it to the cranium. Withdrawal of fluid causes dilatation of the venous sinuses with increase in the weight of the brain, which is responsible for the traction. This is borne out by the fact that bilateral jugular compression causing intracranial venous stasis aggravates the headache. The headache following a lumbar puncture is similar in type and mechanism, and is due to prolonged leakage of fluid through the dural puncture.

CLINICAL SYNDROMES

Histamine Cephalgia or Horton's Syndrome is characterized by a unilateral headache of short duration, usually persisting less than an hour. It is described as constant, excruciating, burning or boring. It commences and often terminates suddenly, often at night, sometimes during daytime, recurring with clocklike regularity week in and week out at a certain hour. It is eased by a change of posture, sitting

up or standing relieves it, reclining or any position causing engorgement of head vessels aggravates it. It involves the eye, temple, neck and face. The distribution is along the branches of the external carotid artery, and in early stages compression of the common carotid or of the temporal artery frequently results in prompt relief.

The headache is associated with profuse watering and congestion of the eye, stuffiness of the nostril, increased surface temperature, perspiration, tenderness, and often a swelling of the temporal vessels. There are no trigger zones. The patients are in the fourth or fifth decade of life. There is no familial or hereditary history. There are no specific causes or precipitating factors. In some cases the use of alcohol precipitates the attack, but abstinence does not result in a cure. There are no scotoma, gastro-intestinal upsets, or relationship to menstrual cycle.

In these patients, it is possible to induce an attack by subcutaneous injection of 0.1 to 1.2 mg of histamine. The induced headache is in every respect identical with the spontaneous attack, can be relieved by injection of epinephrine (1:400,000 sol) or by placing the hand in ice water (i.e. by raising the blood pressure by vasoconstriction).

No specific or hypersensitive states have been definitely found in patients with histamine cephalgia but many patients are relieved by desensitization with repeated small doses of histaminase or histamine diphosphate and are kept free from the attack by an adequate maintenance dose. Some cases are relieved by the use of gradually increasing doses of prostigmine.

Migraine or hemicrania is a disease entity in which headache is a distressing predominant symptom. Headache in migraine is throbbing in character, resembling that produced by histamine or fever. In migraine there is increased pulsation of the temporal artery and the amplitude of pulsation corresponds to the intensity of the headache. Ergotamine tartrate which relieves the headache of migraine does so because it causes a decrease in the amplitude of the temporal artery due to local vasoconstriction. It appears that headache in migraine is due to the dilatation and distension of the cranial arterial walls. Pressure on the common carotid artery during an attack of migraine reduces the severity of the pain and in certain cases ligation of the temporal artery has given freedom from pain in subsequent attacks. Migraine headache is associated with visual aura, scotoma, hemianopia, unilateral paresthesia, and speech disorders, which suggest cortical disturbance and involvement of intracranial arteries. Ligation of middle meningeal artery has given relief in some cases of deep seated temporal pain. It is suggested that for the migraine headache the extracranial and possibly dural branches of the external carotid artery are responsible, while for the histamine and fever headache the cerebral branches of the internal carotid, basilar and vertebral arteries at the base of the brain are primarily responsible.

Headache in arterial hypertension is a common but inconstant symptom. Raised blood pressure in itself is not responsible for headache and the intensity of headache when it occurs does not correspond with the height of arterial pressure. It may be present when the pressure is relatively high, moderate, or low. The high blood pressure patients, who suffer from headache, have always been subjects of chronic headache during periods of fatigue and stress. The mechanism of headache in these cases is identical with that operating in migraine, i.e., the headache results from the dilation and distension of certain branches of the external carotid artery. The attacks of headache in high blood pressure can be relieved by ergotamine tartrate, by pressure on the temporal, frontal, supraorbital, postauricular or occipital artery, by ligation of the middle meningeal or the temporal artery, by thiocyanates, but it is not relieved by increasing the intracranial cerebrospinal fluid pressure.

We saw above that the headache and maximal distention of the cranial arteries occur not immediately after the injection of histamine, when the effect on the contractile state of these vessels is greatest, but some time later when the blood pressure returns to its normal level. It is at this time that the walls of the cranial arteries react to the mounting pressure and headache becomes associated with a level of blood pressure which is ordinarily associated with comfort. The relaxation of the arterial wall and the level of blood pressure are two essential factors in histamine headache. High blood pressure is a necessary but not a sufficient factor in headache of arterial hypertension, contractile state of the arterial walls, which varies in different subjects and under different circumstances of stress, fatigue, emotion, etc., is the essential factor. If the blood pressure is high, a relaxed artery will be more stretched and so the liability to headache will be increased and the pain will be greater.

Headache in intracranial tumour—It is generally believed that headache in brain tumour is due to the stretching of the parietal dura from increased intracranial pressure. Experimental evidence is against such belief. Elevation of intracranial pressure in normal subjects to abnormally high levels fails to cause headache. Headache can be induced by lowering of intracranial pressure by withdrawal of CSF but not by raising the pressure even to a high level of 550 mm. Headache associated with either decreased or increased intracranial pressure results from traction upon or displacement of pain-sensitive intracranial structures and is independent of generalised intracranial pressure changes.

Brain tumour headache is a deep, aching, steady, and dull nature. It is not rhythmic and seldom throbbing. It is usually intermittent, sometimes continuous. It usually does not interfere with sleep. It may be worse in the morning. It is aggravated by coughing, sneezing, or straining at stool or by changes in posture, or by onset of a minor infection. It is moderate in intensity, sometimes severe but rarely intense, as that of migraine, ruptured intracranial aneurysm, or

meningitis, and is usually relieved by acetylsalicylic acid or cold packs applied to the scalp. The pain is not associated with nausea, and vomiting is present only when medulla is displaced or compressed.

Headache in brain tumour is produced by traction upon intracranial pain-sensitive structures, chiefly the large arteries, veins and venous sinuses and certain cranial nerves, either local traction upon the adjacent structures, or distant traction by extensive displacement of the brain, either directly by the tumour or indirectly by internal hydrocephalus. From this it follows that a small tumour involving the tentorium may cause intense headache, while a large tumour not affecting the pain-sensitive structures may be quite painless. Scalp tenderness has also some localizing value in brain tumours.

Psychalgia or Psychogenic pain — When a patient complains of pain or headache and in whom on complete examination one fails to discover any causal physical disease, injury or any physiological disorder of bodily function, and in whom one is justified in holding that none of these factors is responsible for the pain, the pain is considered to be psychogenic, functional, or hysterical. There is no doubt that to the patient the pain is real, but it does not possess the sensory quality associated with physiological pain. It rather depicts complex states of mind, emotionally toned ideas better described as anxiety, grief, anguish or distress. There is an obsession or fixed idea of pain and the patient uses the word pain in the absence of a suitable word to express her agony. The subject is usually a young or middle aged woman, well nourished and healthy, who has suffered from 'most agonising headache' for a number of years without anybody discovering the cause or helping her in any way. The description of the headache is in the superlative terms, usually terrifying analogies, conceptual rather than descriptive, most graphic, and highly gratifying to the patient. The dramatization of the situation is striking. One might say that the patient takes delight in her anguish. There is no relief from any therapeutic recourse, except temporary relief at the onset from any treatment which works as an effective suggestion.

Differential Diagnosis of Headache

A thorough clinical history is imperative. A careful analysis of details regarding (1) intensity, (2) quality, (3) site, (4) tenderness, (5) effect of pressure over chief arteries and veins, (6) effect of change in position of the head, (7) duration, (8) time of onset, day, week, month, season, (9) periodicity, (10) age at onset, (11) associated symptoms, vertigo, nausea, vomiting, photophobia, insomnia, depression, visual disturbances, (12) factors causing aggravation or relief, (13) familial and hereditary history, (14) infection or injury to head, eyes, nose, ears, teeth, and a complete physical examination, including that of the fundi, urine, blood (W.R., leucocytosis), blood pressure, and cerebrospinal fluid, will usually show the cause of any headache which is of clinical importance.

EMERGENCY MANAGEMENT

ITS SURGICAL ASPECTS

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The recent disturbances in Bombay, (September 1946), flooded our hospital with numerous cases which have made us richer in experience and I might say justifiably prouder for the good results we have been able to achieve by an organised teamwork. The fundamental difference in work of this nature from our usual routine work is that we are short of everything—time, material, patience and men. It is scarcely comparable to the two or three emergency operations that one may be called upon to do ordinarily within a short space of time. It is therefore very necessary that utmost economy be exercised in the use of all the things while treating these patients. In the first series of 159 cases studied it will be easily realized that although some of them were admitted in small batches, there were times when the overwhelming number of admissions completely upset the organised approach.

The injuries are grouped under four main heads —

(1) Head injuries, (2) Abdominal injuries, (3) Thoracic injuries, and (4) Miscellaneous injuries.

The injuries were mainly of three types either—bullet-wounds, stab-wounds or blunt injuries due to stones, sticks, etc. Table I describes them in detail.

TABLE I

		Died	
<i>Head Injuries</i>			
(a) Bullet Wounds	1		
(b) Blunt Injuries	39		
		40	2
<i>Abdominal Injuries</i>			
(a) Stab Wounds	42		
(b) Bullet Wounds	4		
		46	10
<i>Thoracic Injuries</i>			
(a) Stab Wounds	53		
(b) Bullet Wounds	2		
		55	12
<i>Miscellaneous Injuries</i>			
		18	2
Total		159	26

1 *Head Injuries* As far as the head injuries were concerned the main treatment adopted was only the routine conservative treatment and operations were done only in two cases of depressed fracture who expired after the operation.

2 *Abdominal Injuries*—These were the most important and every one required an urgent surgical interference. In our series

profusely and died of shock almost all these cases were saved. One case of compound fracture of the femur for which Kirschner's wire was passed also died of severe shock. Most of the wounds were debrided and sutured while fracture cases were plastered with sulphonamide powder in the wound.

Two cases of injury to the left arm have been very interesting in that both of them developed an aneurysm following the trauma.

In the first case, following a stab wound of the left arm the patient was discharged about the seventh day when the wound had healed. Two days later the patient was readmitted for bleeding from the wound which occurred quite furiously. Packing was resorted to. Two days later on examination an aneurysm of the brachial artery was detected with marked thrill and bruit. On exploring, the sac was found to be adherent and was very diffuse. In spite of a tourniquet and a proximal ligature, bleeding re-started and packing was done. Two days later the patient started bleeding for which an exploration was done but as the patient had already lost lot of blood, tight packing was done. A week later, at the fourth operation, a proximal and distal ligation was done and still the wound had to be packed. The wound healed and the aneurysm was cured but the ulnar nerve had been damaged.

In the second case there was a penetrating wound from the left supra-scapular region going to the axilla and forming a haematoma there. At the first exploration, as there was severe bleeding and shock, packing alone was done. As gangrene was threatened the pack was gradually removed. The wound healed but he started getting burning pain in the extremity and was given a course of nicotinic acid, Vitamin B₁, and cobra venom injections. In a few days he showed a pulsating swelling in the axillary region and at an operation. Later the sac was excised after proximal and distal ligation.

Bullet wounds - 13 casualties were due to bullet wounds. All the bullet wounds of the abdomen were fatal and three of them following an exploration. In the first, a child of 4 years, there were two gastric perforations and in spite of suturing and removal of the bullet he died.

In the other two cases there were multiple perforations of the small intestine as many as six and they died after three to four days. The freakness of Nature was well illustrated in a case where the bullet passed through and through from one malar bone to another without causing any disability.

Transfusion and operation are urgently necessary. Often the gunshot wound should be excised and enlarged at the place of entry. A suction apparatus is essential. In dealing with tears of the mesentery, Ogilvie (1944) advises no small ligatures, no catgut, and no stitches. The arteries should be identified and tied with fine thread. To stop liver haemorrhage the best method is to plug the rent with omentum, and oversew with a few catgut sutures.

The bullet wounds of the extremities were attended to later after the more urgent cases were operated upon. Screening, followed by marking of the position of the bullet on the skin, was done in all these cases before operations.

The improved results in this series of cases can be attributed to better organisation, free administration of blood and plasma, penicillin and probably that a majority of our patients were well built and therefore stood the operation better

SUMMARY

- 1 Abdominal stab wounds can be saved by proper treatment
- 2 Chest wounds should be treated on conservative lines
- 3 Proper pre-operative and post-operative treatments are as important as the operation
- 4 Blood and plasma transfusions given immediately help in lessening the mortality
- 5 Penicillin in all the cases undergoing major abdominal operations has reduced incidence of peritonitis

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Dr K G Munsif suggested a mobile X-ray Unit to be kept in the operation theatre

Dr R. G Dhayagude thanked the members of the staff for the whole hearted co-operation received by him in the management of two important emergencies which visited the hospital recently. He stated that the object of Dr Jadhav's paper was to place before the Society the plan which has been evolved after consideration of the experience obtained in these two emergencies. The object of making one ward empty to receive the casualties was to concentrate the staff in one place. This ward would be given additional equipment, nursing and labour staff and it was expected that the casualties would be better looked after than when they are scattered in different places.

The object of restricting the number to 25 of the casualty cases per Surgeon was to see that only the Surgeon on emergency duty on that particular day is not over-taxed. It would be difficult to say as to how long the Physician or Surgeon may have to stay at the premises. Effort would be made to see that they would not be required to remain unduly long. There are many other aspects of this question which were purely of an administrative nature and therefore have not been placed before the Society such as the procurement of foodstuffs, chemicals, medicines, transport facilities, etc. For the purpose of resuscitation the Hon Assistant Physician will be first summoned, but if the emergency is prolonged, then the Honorary Physician will also be required to give a helping hand. It is hoped that with the co-operation that is being received, the Hospital will be able to manage even more severe emergencies should they unfortunately arise than were experienced during the last few months.

TREATMENT OF THYROTOXICOSIS

A DISCUSSION ON PRESENT POSITION

J C PATEL, M D

and

R G GINDE, M S

K. E. M Hospital, BOMBAY

Dr J C Patel in opening the discussion on the present position of treatment of thyrotoxicosis said

"Before the advent of thioracil, the physician's part in the treatment of thyrotoxicosis was to diagnose the disease, to prepare the patient by a conservative treatment for a subtotal thyroidectomy, to advise as to the expediency of an operation and to treat thyrocardiosis and post-operative complications. With the advent of thioracil, a much larger number of cases of thyrotoxicosis can be tackled by a physician.

Thyrotoxicosis should be clearly divided into (1) diffuse hyperplasia with toxic manifestations and (2) adenoma with toxic effects (toxic adenoma). The former is due to the effect of the (hypothalamic region or anterior pituitary) body on the thyroid, whereas the body is affected in the latter case by the thyroid. In neither case, have the causative factors been defined.

The treatment of hyperthyroidism is usually surgical, medical, irradiation or a combination of them. Medical or conservative treatment (without thioracil) has too often been ill-defined as consisting of rest and iodine. Focal infection coincidental with Graves' disease requires correction but precipitous action is hazardous. Freedom from excitement is necessary. Late hours, tea, coffee, condiments, spices, alcoholic beverages and smoking should be forbidden. The patient should have a diet sufficiently high in calories so as to gain in weight, one that is high in proteins and carbohydrates consisting of bread, butter, cereals, dairy products, fruits and vegetables in maximum quantities as also vitamins and liver extracts. The patients in question tolerate quinine with beneficial results. It is advisable to give them iodine in some form. Phenobarbital is a good sedative. Psychotherapy is of the utmost importance to produce calmness of mind. In hyperthyroidism, there is negative calcium balance (Puppel et al 1945) and osteoporosis of the bones, the calcium requirement being trebled. The administration of calcium, phosphorus and vitamin D is indicated to replace the loss caused by hyperthyroidism. It is also helpful in preventing thyroid crisis and in preparing the patient for uncomplicated thyroidectomy. It should be given in the form of calcium diphosphate with vitamin D as it is in this form that it is most easily absorbed and utilised.

Sulphonamides, sulphones (promizole), thiourea and a number of other compounds suppress thyroid activity in animals by preventing the synthesis of thyroxine. They increase the size of the thyroid, decrease the colloid and so produce changes similar to a goitre and

* A discussion at the 65th Meeting of the Seth G S Medical College and K. E. M Hospital Staff Society, Bombay, on November 9, 1946, with Mr R N Cooper in the Chair.

hence they are called goitrogenic drugs Astwood (1943, 1944) after a study of about 120 compounds used two, thiourea and thiouracil to treat thyrotoxicosis As soon as thiouracil became available it displaced thiourea because the latter caused certain objectionable side-effects—halitoses, vomiting and conjunctivitis and was perhaps more toxic Methyl-thiouracil (Leys 1945) is considered less toxic than thiouracil Other drugs like thiobarbital and substituted thiouracil await clinical trials

Mode of Action—Thiouracil acts by interfering with the thyroid activity by preventing the gland from taking up iodine from the circulation and incorporating it into the thyroid hormone Thiouracil produces a hyperplastic but non-functioning goitre The effects produced are similar to those consequent on the removal of the gland Figuratively speaking, thiouracil produces a chemical thyroidectomy In response to a lowered level of thyroid hormone in the blood, the anterior pituitary increases its production of thyrotropic hormone, the result being a compensatory hyperplasia of the thyroid (a frustration goitre due to relative hypothyroidism) which nevertheless does not respond by increased activity, as thiouracil prevents synthesis of the hormone Such is not the case if the anterior pituitary has previously been removed Actually, lowered metabolic rates result The pituitary itself shows hyperplasia and histological changes similar to those seen in thyroidectomised animals Delay of thiouracil effect by previous iodination is due to excess iodine stored in the thyroid gland which must be exhausted before thiouracil can act and manifest its result (Palmer 1945) Iodine given concurrently with thiouracil does not appear to alter the effect of the latter, provided the thiouracil is given a few hours earlier Thiouracil does not act on whatever may be the cause (which is yet to be found) of thyrotoxicosis Enlargement of thyroid due to thiouracil therapy can be reduced by administration of thyroxine

Dosage—(1) *Initial Dosage*—Experience has shown that thiouracil should be administered in the initial stage of treatment in three or four divided doses at equal intervals during waking hours The total daily dose formerly varied from 0.1 to 2.0 gm The majority of investigators used either 0.4 gm to 0.6 gm per day and since results were as satisfactory at the lower figure as at the higher, it seems that the initial dosage per day should preferably be 0.3 gm or 0.4 gm The minimum effective doses of thiouracil have not yet been worked out

(2) *Maintenance Dose*—A smaller dose of the drug is sufficient to preserve its effect than what is necessary to bring the disease under control The dosage should be progressively decreased because doses which in early stages sufficed to maintain control may later produce symptoms and signs of overdosage Adjustment of dosage to anticipate decreasing requirements is the main problem of maintenance therapy The dose may be reduced to 0.2 gm, 0.1 gm, or 0.05 gm per day, the criteria for reducing the dosage being weight and basal metabolic rate

Effect of Overdosage—Gross overdosage shows itself by an increase in the size of and sometimes painful goitre Weariness and

depression sometimes appear suddenly Plasma cholesterol may be elevated There may not be gain in weight, or B.M.R. may become subnormal This type of overdosage may occur during maintenance therapy and can be avoided by reducing dosage to the minimum Effects of overdosage should not be confused with the toxic effects of the drug

Effects—No case of thyrotoxicosis is refractory to thiouracil if the treatment is continued for a sufficiently long period, because it is possible that clinical response to the drug may not be felt for several weeks, (60 to 100 days) after the treatment has been started Its effect is particularly delayed if iodine has been previously administered or if the gland was large and soft, as also in large toxic adenoma (because such glands have large store of iodine) Some even appear to become worse for a time with thiouracil therapy In the majority of cases good effects are often apparent in less than 10 days and normal conditions are usually reached within 60 days from the commencement of the treatment Thiouracil exerts beneficial effects (Barr and Shaw 1945) on most of the signs and symptoms of hyperthyroidism Some symptoms seem to be more readily susceptible to the drug than others Symptoms such as goitre and exophthalmos believed to be extrathyroid in origin are little if at all affected, eye-lid spasm and concomitant lid-lag disappear in most cases giving a false clinical impression that exophthalmos has greatly improved though it actually increases in some cases Changes in the size of thyroid gland are not uniform but mostly minimal The gland may even increase in size Sweating, flushing and diarrhoea disappear first Nervousness decreases to such an extent that calm demeanour may be considered abnormal Cholesterol rises to normal Increase in weight and fall of B.M.R. occur rapidly, long before tachycardia subsides Failure to realise this last-named effect has probably caused some patients to be classified prematurely as thiouracil-resistant (Himsworth 1944) The fall of B.M.R. is not proportionate to the dose of thiouracil, especially in toxic adenoma

Toxic Effects—The result of the treatment with thiouracil of 5,745 patients was analysed by Winkle et al (1946) in order to ascertain the toxic effects The summary is given below

The principal toxic reactions observed following medication with thiouracil were granulocytopenia (agranulocytosis), leucopenia, drug fever and dermatitis No less than 27 other reactions were recorded of which however, only eight were observed in more than two cases This suggests that most of the reported side-reactions other than those specifically named, or the others mentioned later, were not related to thiouracil medication at all Approximately, 13 per cent of the cases may be expected to show some adverse reaction to thiouracil therapy The appearance of jaundice, purpura and anaemia has been reported and should be watched for, and if observed, calls for a careful evaluation of the clinical condition of the patient before thiouracil therapy is resumed

Granulocytopenia occurs in about 25 per cent of cases and is the most serious complication of thiouracil therapy There were twenty-one deaths all attributable to agranulocytosis establishing a mortality

rate of 0.4 per cent for the entire series. This reaction tends to occur in the early weeks of the treatment and in 80 per cent of the cases it was noticeable by the twelfth week of therapy. No relationship to the dose of thiouracil was apparent.

Leucopenia was seen to have an incidence of 4.4 per cent early in the treatment, 75 per cent occurring in the first eight weeks, not being however, related to dosage. Drug fever had an incidence of 2.7 per cent, noticeable very early in the treatment, 85 per cent occurring in the first four weeks, but unrelated to dosage. The reactions occurring early tended to be more severe than those occurring later. Skin reactions had an incidence of 3.3 per cent, urticaria being the most common, but there was a wide variety of other dermatoses as well. None were deemed serious but caution is advised in continuing therapy in the presence of these complications. Three-fourths of the investigators were of the opinion that the incidence of adverse reactions to thiouracil was less than the incidence of the complication arising from present methods of treatment. It should be emphasised that patients receiving thiouracil therapy need being carefully watched, especially during the first twelve weeks of the therapy, and should be instructed to report immediately to their physician if any adverse symptoms such as sore throat, fever, coryza or malaise are experienced and in that event, to stop taking the drug.

Methods to prevent it — Careful surveillance of the patient and proper selection of cases are important preventive factors. It has been the usual practice to initiate the treatment in an hospital particularly in severe cases, (thyrocardiacs), but it can also be carried out in the case of an ambulatory patient, dosage of the drug given to him being sufficient only for four days treatment. The American Medical Association requires the printing of a warning on the label of the bottle apart from that which the attending physician is required to give to the patient. The treatment should be begun with a small rather than a large dose. It is safer and equally effective. Close, detailed and continuous supervision is indispensable during the first two months of the treatment. In the follow-up clinic, the patient should be warned that the development of fresh symptoms such as sore-throat, fever or a rash is an indication to stop the drug and report for treatment immediately. This warning is even better and more practical than repeated blood counts (Mulengracht 1946). This is because the blood count may be normal one day and severely leucopenic the next, and in any case leucopenia may cease spontaneously even though the drug is continued. There is no satisfactory evidence that administration of liver extract, pantothenic acid, pyridoxine, folic acid, vitamins or pentanucleotide aid in preventing such reactions or change the outcome of the disease. The best treatment of agranulocytosis apart from stopping of the drug immediately, in early recognition and probably large doses of penicillin. The drug has a predilection for bone marrow. The concentration of the drug in bone marrow is much higher than elsewhere in the body. A thiouracil substitute with a greater predilection for thyroid and lesser for bone marrow should be sought. It was not possible to obtain re-

liable figures on the incidence of remissions induced by thiouracil. By remission is meant absence of symptoms and a basal metabolic rate within the normal range after the drug had been discontinued. The majority of investigators did not terminate treatment except in those cases in which thyroidectomy was performed. In such cases there was no way to determine the duration of remission. Those who develop toxic symptoms are considered hypersensitive to thiouracil as they might conceivably be to any other drug. In the majority of such cases the sensitiveness disappears as the treatment is continued. In a few cases it disappears on discontinuance of the drug or by decrease of the dose. When the drug is readministered, the symptoms do not appear. The patients who relapsed after withdrawal or reduction of the dosage always responded promptly when the drug was readministered, or the dose increased.

Other Uses of Thiouracil—Besides the use of thiouracil in thyrotoxicosis it is effective in acute thyroiditis (King and Rosellini 1945) and in angina pectoris (Raab 1945) and congestive cardiac failure. Thiouracil is definitely an established pre-operative remedy for both the hyperplastic and toxic nodular goitre. By its use before an operation there is a decided economic advantage in that it reduces the average stay from weeks to 7—10 days (Bartels 1945). It also reduces surgical risk.

Chances of Survival with Surgical Thyroidectomy and with Chemical Thyroidectomy with Thiouracil in Thyrotoxicosis—The mortality from thyroid surgery varies with the surgeon and degree of pre and post operative care. Mortality at the Lahey Clinic was 0.67 per cent, but in the last 100 cases with thiouracil as a pre-operative measure, it was nil. Of Keynes (1946) (L.C.C.) less than one per cent, of K.E.M. Hospital (Munsif 1944) 11 per cent, which includes all cases of thyroid including colloid goitre. Moreover, major complications such as post-operative thyroid crises, parathyroid tetany and injury to recurrent laryngeal nerve may follow the operative and relapses and residual thyrotoxicosis are quite common (about 30 per cent) myxoedema may also occur. The deaths from agranulocytosis after treatment with thiouracil were 0.4 per cent in a series of 5,745 cases, and toxic reactions in 13 per cent of the cases, and this is probably a maximal figure since it covers early days when experience was being gained. If one concentrates on the toxic symptoms occurring during thiouracil therapy, and perhaps to a lesser extent with methyl-thiouracil therapy, one is inclined to underestimate the importance of the discovery of a drug with such a profound and radical influence on thyrotoxicosis. There is no doubt that results achieved by surgery in the Lahey Clinic or in the hands of Joll are impressive, but most patients prefer medical treatment. They can return to work once the control has been achieved. It is true that supervision is more difficult and takes longer but the patient rarely objects to this and those in a hurry can still take the short cut offered by surgery, but even then only after preliminary preparation with thiouracil. In the treatment of thyrotoxicosis Bierwaller and Sturges (1946) commented that "thiouracil may be used in about one-third of the thyrotoxic patients only, as a pre-operative

treatment, since these patients of nodular goitre might develop a malignant condition. Another 7 per cent will require thyroidectomy on account of complications which occur during thiouracil therapy. About 15 per cent of the patients with thyrotoxicosis will leave the physician's care for personal reasons which are the instances related to difficulties encountered in thiouracil therapy. In the remaining 45 per cent of the total group made up of those with toxic hyperplastic goitre thiouracil therapy may be continued till the patient experiences a persistent drug-induced remission."

Thiouracil is an effective but potentially dangerous drug entailing serious complications and needs therefore caution in its use. It promises a bright future for patients with thyrotoxicosis.

The following are indications for thiouracil therapy

(1) Thyrotoxicosis with diffuse hyperplasia, particularly in the very young, the very aged, and debilitated, (2) Toxic adenoma with complications unfavourable for surgery i.e. thyrocardiacs, fibrillation, hypertension, diabetes and decompensation. Operation is inevitable if cancer is suspected, (3) Those with extra-thyroid factors conceivably responsible for thyrotoxicosis, (4) Recurrence after subtotal thyroidectomies, (5) Thyrotoxicosis with pregnancy, diabetes.

Indications for Surgery in Cases of Hyperthyroidism

(1) Toxic adenoma where malignancy is suspected."

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Dr R. G. Ginde, said —

"My friend, Dr J. C. Patel, in initiating the discussion on the present position as regards the treatment of Thyrotoxicosis, has presented at length the role of Thiouracil and has incidentally almost eliminated surgery from the field.

Before discussing the subject however, I may be permitted to make a few general remarks. Goitre cases are very often seen by Surgeons because of the prominence of or swelling in the neck. Toxic goitres approach the Physicians for the different systemic toxic manifestations. But at times, they may also be seen primarily by the Ophthalmologists, Psychiatrists, Gynaecologists and others for symptoms of their respective specialities. And in these cases except those with a fairly clear cut and well-established picture of the disease, the diagnosis largely depends on the help of the Pathologist and the Biochemist. I therefore feel especially happy that we are

meeting here today to review the present status of the treatment of this condition. The next point I would like to place before you as a corollary to this is, that, no matter who sees these cases first, they should be studied and treated jointly by the Physician and the Surgeon. And I do hope that before long we shall have another occasion to discuss this subject wherein, a review of cases from our own hospital—cases though few but properly studied, carefully investigated, treated and followed up—would be presented.

Mention has already been made about the management of Thyrotoxicosis before the advent of Thiouracil. To recapitulate briefly, it consisted of the following:

- (1) Complete bed rest especially in thyrocardiacs and for a shorter period in others followed by gradual ambulation.
- (2) Removal of the patient to an institution away from the usual excitable surroundings with psychotherapy when necessary.
- (3) A high calorie—5,000 calories per day—high protein, high carbohydrate diet with adequate amounts of Vitamins A, B, C, and D, and Calcium di-phosphate.
- (4) Administration of Plasma, Amino-acids, Glucose etc to supplement (3) above.
- (5) Treatment of anaemia.
- (6) Lugol's Iodine for 2 to 3 weeks followed, during a remission when there occurs an improvement in the patient's general condition, slow steady pulse, gain in weight, B.M.R. within $+5$ to $+15$ and a rising blood cholesterol, by subtotal thyroidectomy in one or more stages aided by saline and blood transfusion during the operation.

With such a careful preoperative regime, adequate anaesthesia, judicious team surgery and vigilant post-operative management, the operative mortality of these cases in some of the leading clinics has been as low as 0.27 to 1.5 per cent¹ for primary hyperthyroidism and not more than 4.8 per cent² in thyrocardiacs and even in those with recurrent hyperthyroidism. In these clinics, the use of thiouracil in the pre-operative preparation has not significantly affected the mortality rate. It has however, helped to make the operation less risky, diminished the number of stage operations and has shortened the period of hospitalisation to 7—10 days.

Today the opinion prevails amongst those most experienced with the disease that subtotal thyroidectomy is the treatment of choice, for it most rapidly, most certainly and most safely restores the patient to a state of economic efficiency. Thiouracil will supplement but not supplant surgery in the treatment of toxic goitre³⁻⁴. But from the evidence that has accumulated from the reports of large series of cases treated with Thiouracil with proper control, over a period of two years or so, it is fair to say that this drug is likely to produce the same result as is obtained by surgery without subjecting the patient to the risk of a major operation. Thiouracil is not the ideal drug for this purpose because it actually increases the histologic abnormality of the disease by interfering with the synthesis of the hormone and does not affect the underlying aetiology of thyrotoxicosis. The goitre itself does not disappear. Besides it may be accompanied by dangerous and at times even fatal toxic complications and render surgery also more difficult.

So, from the present state of knowledge about this disease, con-

trolled thlouracil therapy as suggested by Dr J C Patel should be administered in the following types of cases —

- (1) Primary diffuse toxic goitres of short duration
- (2) Thyrotoxicosis in elderly debilitated subjects and with de-compensated heart (Thyrocardiacs)
- (3) Hyperophthalmic type of Thyrotoxicosis
- (4) Hyperthyroidism complicated by (a) Diabetes (b) tuberculo-sis (c) Pregnancy
- (5) Those showing symptoms during or after a severe illness
- (6) Recurrent hyperthyroidism, and
- (7) Iodine fast goitres

Whereas surgery should be resorted to in the following —

- (1) Toxic adenomas or nodular toxic goitres because of (a) danger of malignancy (b) their slow and delayed response to thlouracil (c) Cosmetic reasons on account of the large lump in the neck and (d) when pressure symptoms are present
- (2) Failure of thlouracil treatment because of (a) Thlouracil refractory cases⁵, though these are rather rare (b) Occurrence of repeated severe toxic manifestations during treatment (c) Patient not being able to co-operate because of distance, economic or other reasons (d) When sometimes there is sudden increase in the size of the thyroid with marked pressure symptoms during treatment

These cases may be as high 40 per cent of total toxic goitres³

When surgery is decided upon, patients should be prepared with Thlouracil first and Iodine should be given alone two weeks just before the operation

I may end up by reviewing certain aspects of thyroid surgery which might help us in lowering the operative mortality and improving the ultimate results in our cases

The ideal subtotal thyroidectomy⁶ must be (1) as anatomic as possible respecting and preventing damage to important vessels, nerves and organs (2) as physiologic as possible resecting most of the thyroid parenchyma so that the chances of recurrence are minimal (3) avoiding important post-operative complications such as haemorrhage, acute hyperthyroidism, tetany and myxoedema

These can be achieved by —

- (1) Carefully selecting the patients after adequate preparation
- (2) Suitable anaesthesia
- (3) Proper position of the patient on the table
- (4) Low collar incision giving adequate exposure and an effective cosmetic result
- (5) Cutting the infrahyoid muscles instead of retracting them, at a level higher than that of the skin incision to preserve their nerve supply and to prevent an adherent scar
- (6) Gentle handling of the thyroid gland itself (using if possible Lahey's double hooks)
- (7) Careful haemostasis by (a) ligaturing all the significant thyroid vessels before resecting the gland This⁷ incidentally shortens the operation time, gives greater insurance against post-operative haemorrhage, makes possible a more accurate estimation of the size of the thyroid remnant and affords an opportunity to see and preserve the parathyroids, (b) using electrocoagulation for

resecting the gland and (c) by suturing the remnants to the sides of the trachea with mattress or crisscross sutures

In connection with toxic goitres, it should be noted that, sub-involuted thyroids, thyroids prepared with thiouracil only, hypertension especially in long standing toxic adenomas and a rise of blood pressure associated with anaesthesia may produce increased bleeding during operation

(8) Avoiding injury to recurrent laryngeal nerves by their routine exposure Lahey has shown that since adoption of this procedure in all operations on goitres, the incidence of recurrent nerve paralysis is decreased to less than 0.3 per cent⁸ (9) The use of linen (No 80) for suturing, as it produces less tissue reaction (10) Operating in stages if the patient's condition demands it (11) Employment of drainage when the ideal dry wound cannot be accomplished and finally by (12) Vigilant post-operative care especially with a view to prevent acute hyperthyroidism by the use of (a) Thiouracil 0.6 gm per day for 3 to 4 days with 50 to 100 min of Lugol's solution in saline (b) Oxygen in a tent or by a B.L.B mask (c) Continuous glucose saline drip with 100 Gms of glucose per day and (d) Morphine, barbiturates or other sedatives

Case Report—R V Indoor No S/13501, aged 43, male Hindu, from Karachi was admitted to the K.E.M Hospital on 1-11-1945 for progressive loss of weight, tremors of the hand, swelling in the region of the thyroid gland, bulging of the eyeballs and palpitation for about 5 years. He started rapidly losing weight and then developed tremors of the hand. He was feeling increased warmth of the body surface also. After about a year or so he noticed an enlargement in the region of the thyroid gland which went on increasing. Sometime later, he noticed that his eyeballs had become more prominent. He went to a doctor who gave some iodine preparation, which he was taking till about 2 weeks or so before seeking admission to the K E M Hospital. He had taken thyroid extract tablets and had become worse and therefore given them up. With iodine he was feeling much better. There were no pressure symptoms except that he had slight hoarseness of voice of recent origin and he complained of palpitation.

On examination, he had a diffuse but nodular enlargement of the whole of his thyroid gland, firm in consistency and moving freely with deglutition. Maximum girth of the neck was 16.8 inches. There was marked proptosis especially of the left eye with loss of convergence of the eyeballs, Tremors of the tongue and fingers. Temperature 98°F, Pulse 100 came down to 78 per min. Respiration 24. Weight 122 lbs, blood pressure 142/86 mm Hg. Blood picture showed R B Cs 5 millions, Hb 90 per cent, W B Cs 6,250. Diff Count P 60 per cent, L 34 per cent—M. 6 per cent, E Nil. B M R could not be done as the machine was out of order. Blood cholesterol was 123 mgms per cent and then rose to 152 mgms per cent with treatment. The hippuric acid test showed the benzoic acid excretion of 2.21 gms increased to 3.02 grms under treatment, the weight increased to 134 lbs. He was given a high protein, high caloric diet + 100 c.c of 25 per cent glucose with vitamin C 500 mgms daily.

Injection of Liver Extract 4 U.S.P units and Vitamin B complex on alternate days and Iron He was given 0.6 gm of Thioracil per day in 6 doses 2 hourly from 20th November 1945 His weight, blood cytology, blood pressure, pulse and girth of the neck were recorded every 4 days, and when his weight increased to 134 lbs, he looked calm and collected, had almost a normal blood cytology, pulse rate of 78, blood pressure 128/90 and girth of the neck 15.9 inches, he was operated on 19-12-1945 under Avertin and N-O anaesthesia, saline 500 cc and blood 300 cc were given during operation by the drip method During operation, there was unusual bleeding in spite of ligaturing the thyroid vessels on the right side before resection His pulse rose to 160 and so only right sided lobectomy was done His condition after the operation was satisfactory, pulse being 120 min He was given morphia gr $\frac{1}{2}$ and O was given continuously afterwards by a nasal catheter Next day his condition was fairly good Patient was quite conscious and cheerful—Temp 99° Pulse 96 But he complained of some discomfort in the neck, thirst and headache Glucose 100 cc with Lugol's solution 2 cc was given His temperature after 2 hours was 102°F, Pulse 106 So glucose saline was given After 200 cc had been given he became rowdy and delirious, then temperature rose to 104°—107°F Pulse 160 and more till it became imperceptible and he died of acute thyroid crisis in a comatose condition at 6 a.m. on the 24th December, 1945, in spite of the above treatment

Comments - Here was a case who was very carefully studied and investigated jointly in conjunction with the Physician He was treated with full doses of Thioracil for nearly a month which is sufficiently long for most of the severe cases of Hyperthyroidism And there was such marked improvement in his general condition, weight etc, that he was thought quite fit for the operation (by the surgeons in charge) It is quite possible that he could have been treated for a longer time with maintenance doses of Thioracil Secondly although stage operation was done, no pre-operative iodine was given and similarly Thioracil was not administered after the operation Whether saline given on the next day, actually induced the thyroid crisis is difficult to say In my opinion it was the saline reaction that led to thyroid crisis Anyway the unfortunate result in this case should make us take even greater care in the management of these cases in future "

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DISCUSSION

Dr Z J Joseph said that there was always a certain amount of controversy about the treatment of thyrotoxicosis by Surgery and Roentgen Rays The fear in adhesions after X-ray therapy, he

added, was not justified, in view of the modern high voltage apparatus. He added that roentgen rays had a beneficial effect in the sympathetic nerves which were irritated in the disease. He further added that other glands of internal secretion were always affected and their irradiation might benefit the patient. In cases coming for autopsy, it had been observed that in 75 per cent, the thymus was enlarged. He then enumerated the indications and the contraindications for X-ray therapy as follows

Indications -- (1) Primary thyrotoxicosis of such a degree that early operation is not necessary (2) Primary thyrotoxicosis in childhood and adolescence (3) Primary thyrotoxicosis which relapsed following operation (4) Primary thyrotoxicosis where operation is refused

Contra-indications (1) Secondary thyrotoxicosis or toxic nodular goitre (2) Primary or secondary thyrotoxicosis with cardiac failure or auricular fibrillation (3) Tracheal displacement on compression (4) Retrosternal goitre (5) Doubtful diagnosis

Dr G M Phadke reported one case of thyrotoxicosis treated with thiouracil, which developed a fatal agranulocytosis

Dr M M Pandya stressed the importance of multiple stage operation in thyroid surgery as a major factor towards the lowering of mortality attending the operation in the institution.

Dr N K Sahar reported a case of thyrocardiac successfully operated upon in England. He was of the opinion that three years, was a short period, for assessing the results of treatment with thiouracil

Dr N F Saher speaking on the anaesthetic management of thyrotoxic patients stressed the importance of taking the pulse rate during sleep, which is he considered a more reliable guide of the basal metabolic rate. He advocated radiograms in two planes to detect tracheal deviation and endotracheal tube to safeguard a clear airway, as these patients stand oxygen lack poorly. He further said that barring chloroform, any other anaesthetic could be used provided the patient was prepared carefully

Dr R H Karmarkar quoted a case of thyrotoxicosis treated pre-operatively with thiouracil, without iodine medication. He said that at the operation the gland was more friable and consequently haemostasis more difficult. At the time he was not aware of the necessity of administering iodine after thiouracil, to render the gland firmer. He compared this observation with a similar one of Bartel (Lahey Clinic)

Dr K A J Lalkaka stressed the importance of psychotherapy in the treatment of thyrotoxicosis because psychic trauma is one of the factors in the etiology of the disease

Dr A E de Sa agreed with Dr Karmarkar regarding the friability of the gland following thiouracil therapy. He described a case in which under treatment with thiouracil developed oedema of the legs on the tenth day, the cause of which he could not ascertain

Dr K G Munsif said that thiouracil therapy was in its infancy and he considered that surgery was still the last word in the treatment of thyrotoxicosis

Dr V P Mehta said that recurrences occurred after partial thyroidectomy as well with thiouracil therapy. He argued that surgery could not replace thiouracil therapy. He cited Hertzler who had shown the value of total thyroidectomy in toxic goitres and recommended it in all the severely toxic goitres needing surgical treatment. Hertzler had further proved that post-operative myxoedema in patients of over 25 years of age did not occur.

Dr J K. Mehta said that psychological elements played a great part in the etiology of toxic goitre for which he advocated adequate treatment. He also added that the disease had a familial incidence and suggested a prophylactic treatment especially at times of physiological stress. He was of the opinion that the cause of death in the case cited by Dr Ginde, was due to saline reaction.

Dr R N Cooper enquired the rationale of Penicillin in the treatment of agranulocytosis.

Dr J C Patel in reply to Dr Cooper said that Penicillin was used as a prophylactic to combat infections of the mucous membranes which occurred commonly in agranulocytosis. He agreed with the various speakers about the toxic reactions of the drug, particularly agranulocytosis which proved fatal in 0.4 per cent of cases. He argued that the occurrence of toxic reactions should not be a deterrent to the use of this drug, especially when good results have been obtained in a large series of cases. He added that if one concentrates on the toxic symptoms occurring during thiouracil therapy, one is inclined to under-estimate the importance of the discovery of a drug which has such a profound and radical influence on thyrotoxicosis.

(Continued from p 120)

investigation. Sixth, scientific work is a social as well as a personal enterprise. All scientists must take on trust a vast body of facts established by their colleagues and predecessors, and it seldom happens that any important field of scientific investigation is monopolized for long by one man. Consequently, the practice of science requires both personal integrity and respect for one's colleagues, tolerance for other's opinions, and determination to improve one's own, and care not to overstate one's case or to underrate that of others. Thus a mental 'climate' is favoured which is a balance of appreciation and criticism"—E F CALDIN

"The maintenance of intellectual integrity, the defence of intellectual liberty, the cultivation of strict veracity and methods of precision, the sharing of new knowledge, the obligation to publish important findings and to include essential references, and the recognition of priority where priority is due—all these are a part of the discipline, in an ethical regard, which men of science observe. Of intellectual standards, the Hippocratic injunction states succinctly 'One must occupy oneself with facts persistently', and 'there are, in fact, two things, science and opinion, the former begets knowledge, the latter ignorance'. As a reminder for the teaching of the clinical schools the latter sentence might suitably be inscribed above the portals of each ward and lecture room"—Prof J A RYLE

Critical Notes and Abstracts

MERSALYL—DAILY USE (See Indian Physician Vol vi, p 97) Mersalyl, mercupurin, salyrgan, neptal, esidrone, or novurit, is commonly used as a diurectic in cases of cardiac oedema. The usual practice is to inject 2 ml every 4th or 5th day. This produces a marked diuresis on the day of injection and some diuresis on the next day, but this is followed by a great deal of retention of water during the following two days. This makes it difficult to make the patient oedema free in a short time. It is known that an average man can metabolize 1 ml of mersalyl without retaining any, this makes it possible to inject 1 ml of mersalyl daily without causing any accumulation of the drug or producing any toxic symptoms. The daily injections can be continued till all oedema has disappeared. The method is to weigh the patient, and measure the amount of urine passed daily, and to go on injecting 1 ml of mersalyl daily till the weight becomes stationary and remains so for three or four days. This may take from 10 to 12 days. I have used it daily for periods even longer than this but if the oedema does not disappear by this time, the cause of oedema will need reinvestigation, and hypoproteinemia, nutritional or vitamin deficiency, presence of chronic infection such as pulmonary tuberculosis, will need exclusion. It must be remembered that the patient continues losing weight for several days after the visible or pitting-on-pressure-oedema has disappeared. Again, in patients with left ventricular failure there may be no visible oedema, but mersalyl injections may remove 10 to 20 lbs of fluid, with resultant remarkable clinical improvement, once the weight becomes steady. The injections may be omitted and restarted again as the weight begins to rise. As a maintenance does some patients may require a regular use of mersalyl for some weeks, months or years.

Daily use of mersalyl is quite free from any dangers, if the indications and contraindications for its use are properly taken into consideration before its use. In restarting mersalyl again, it is well to keep in mind that the fatal outcome which resulted from its use was only in those patients where it was restarted after a period longer than 8 to 10 days, in whom there was a history or definite evidence of renal disease, and where the drug was used intravenously, suggesting that the fatal outcome was more of a nature of a drug anaphylactic shock in nephritic patients. To avoid this, it is best to inject the drug intra-muscularly, to avoid its use in cases of renal disease and the interval between its use should not be longer than 7 days or so. If longer, desensitization with smaller daily doses should be carried out.

BENADRYL—(See Indian Physician, Vol vi, p 47) is widely used as an antiallergic drug. Though it is well tolerated given in dosage recommended it is best to keep in mind that numerous side effects caused by it are reported in the literature. These are drowsiness, sleepiness (countered by benzedrine 5 mg or caffeine 1 grain), nervousness, dryness of the upper respiratory passages, weakness, fatigue, ataxia, facial edema, urinary frequency, nausea, epigastric distress, bad taste,

a tendency to bleed, a sense of relaxation, tingling of the extremities, tinnitus, chilliness, pruritus, faintness, acute hysterical reaction, dilated pupil, stupor, narcolepsy, confusion, blurred vision, sore tongue, pallor, hot flushes, aggravation of allergic state, irritability, palpitation, exhaustion, collapse, somnambulism, dizziness, numbness, cold extremities, muscular-aching, headache and acute melancholia. These side reactions promptly disappear on discontinuance of the drug. Spontaneous asthma and a vaso-spastic condition involving the fingers of the one hand have also been reported from its use. An unusually prolonged reaction to benadryl is reported by Schwartzberg and Wallerson (J.A.M.A. 133 6 393). A man aged 38, on benadryl was taking one to three 50 mg capsules per day off and on, and had taken 23 capsules in 20 days. One week after starting benadryl he noticed puffiness of the eyes, and the occurrence of 3 stools per day, with considerable amounts of flatus. Towards the end of the second week a feeling of tightness was noticed in the arms, hands, and behind the knees. There was numbness, prickly sensations and difficulty in working with small tools, because he dropped them so frequently. Cerebration became slow, and the patient felt weak, groggy and sick. It took about two months for these symptoms to disappear. The patient's symptoms are considered to be intensification of the normally expected action of benadryl. Low blood pressure, and neuritis are reported after the use of those drugs which act by displacing histamine in the tissues (e.g. pyribenzamine, sulpho-namides, histamine derivatives, such as heparamine). Borman (J.A.M.A. 133 6 394) reports the case of a convent nun aged 18, who took 40 capsules of 50 mg each in about 4 days, and became mentally confused, disoriented, lethargic, and behaved in an irrational manner. She recovered completely within forty-eight hours. The author suggests that the mental effects of benadryl (elation, confusion and clouded judgment) may prompt a person to overmedication. Gelger et al (J.A.M.A. 133 6 392) report a case of a woman aged 26, suffering from generalized seborrheic dermatitis, who was given 50 mg benadryl thrice daily. After receiving 300 mg of the drug, she complained of palpitation, dimmed vision, malaise without drowsiness and heartburn with nausea. Following the next regularly scheduled dose of benadryl (making a total of 350 mg) the patient *was found unconscious in bed, cold, pale, and pulseless*. Blood pressure could not be obtained. Injection of $\frac{1}{2}$ ml of 1:1000 sol of epinephrine improved the pulse in 30 minutes and in three hours the patient became normal, with no recollection of what had happened. Benadryl was started again after seven days, under careful observation. Again, after taking 300 mg of benadryl in three days, the patient complained of palpitation, severe malaise, dimmed vision and nausea, and became disoriented and excited, with a weak pulse and marked skin pallor. On discontinuing the drug she recovered in two hours. The authors consider this *an anaphylactic shock-like-reaction of the drug*. Weil reports (J.A.M.A. 133 6 393) a case of a child, aged $3\frac{1}{2}$ years, weighing 33 lbs suffering from hay fever, who was prescribed 50 mg

benadryl morning and at bed time The child was given the drug for 3 days (i.e. 300 mg) During the night of the third day, after returning to bed apparently normal the child woke up about midnight with a severe sneezing attack To alleviate this, 2 capsules (100 mg) of benadryl were given At 12.20 a.m. the child was found sitting up in bed, singing, laughing and starry-eyed He did not obey orders to lie down and remain quiet but instead laughed and acted as though he were drunk There were muscular twitchings of the face and involuntary spastic movements of the limbs Shortly afterwards there was urinary incontinence The muscle movements became worse in ten minutes and the child became quite irrational He 'dove' (dived) from his bed, head downwards on to the floor, and laughed as picked up and put back to bed The speech was slurred 1½ grains of seconal put the child to sleep in fifteen minutes, though the muscular twitchings and athetoid movements continued Several times the child attempted to dive out of the bed during the next three hours After 4 a.m. he slept soundly till 9 a.m. Sleepiness persisted till 4 p.m. when he was considered to be quite normal The child remembered nothing of the night episode Since then he has taken upto four doses per day without any side effects, bigger dose is not repeated The author suggests that the accepted dose of benadryl for children i.e. 2 mg per lb of body weight should not be exceeded

It is best to remember that benadryl shows its maximum clinical response within ten to twenty minutes, and the effects last for five to eight hours Hence, it is not advisable to prescribe the drug more frequently or to repeat the drug within eight hours

Reflections and Aphorisms

"Scientific life is a type of life lived according to right reason *First*, it demands the experience of the senses, not haphazard experience and hearsay evidence, but careful observation and intelligent searching, a mind alert for novelty but trained also in cautious verification. *Second*, it demands that observation shall be interpreted by reason, which brings order into the data of sense, it requires rigorous logic, controlled imagination, intellectual insight, clear analysis, and wide synthesis It requires that we learn about nature from experience (as distinct from spinning myths) and that we interpret that experience by reason (as distinct from merely remembering or applying it) *Third*, it is characterized by a continual interplay of experiment and theory, experiments suggest hypotheses, hypotheses in turn suggest experiments which may verify them. Scientific life, then requires a rational unity of thought and action. *Fourth*, it is a developing tradition neither a code of unalterable rules, nor, on the other hand, a formless collection of varying authenticity devoid of established criteria for judging new developments That is, the scientific spirit will tolerate neither a sterile immobility nor a rootless fickleness, scientific beliefs need periodic overhaul and constant adjustment *Fifth*, as a consequence, scientific life requires freedom freedom of thought, of discussion, of publication, and of

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Original Contributions

PERICARDIAL EFFUSION

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Riolanus (1650) recognised pericardial effusion and suggested paracentesis by the trans-sternal route. A century later, the condition was studied by Senac, Corvisart, Lennac, Morgagni and others. Larrey, Napoleon's surgeon, performed a series of experiments on cadavers and finally elaborated the safest approach to the pericardium by the epigastric route (King).

Williams (1903) described the radiological appearances of pericardial effusion and Roesler (1937) observed that only effusions above 250 cc could be detected radiologically.

Cybalski and Surzycki (1912) and Oppenheimer and Maun (1923) found low voltage in all the leads in pericardial effusion and Gager (1924) reported changes in the S-T segment similar to that occurring in cases of coronary thrombosis. The changes disappeared after the removal of the effusion. These observations were confirmed by Wood and White (1925), Porter and Pardee (1929) and several others. The electrocardiographic changes have been dealt in detail by Scherf (1931), Vender Veer and Norris (1937) and Bellet and McMillan (1938) and others.

This paper is a study of twelve cases observed by the senior author. They were all diagnosed clinically except the last case of non-inflammatory effusion and were confirmed by radiological examination, by aspiration of the fluid or by postmortem. They are aetiologically classified as follows:

	No. of cases
1 Rheumatic infection	6
2 Myxoedema	1
3 Congenital polycystic disease of the kidney	1
4 Unknown causation	
(a) Serofibrinous exudation	1
(b) Haemorrhagic effusion	2
5 Non-inflammatory effusion	1
Total	12

Brief notes of these cases are given below —

1 *Rheumatic infection*

Case (1) Small quantity of effusion completely absorbed by salicylates—N G, male aged 35 years, was admitted on 5-2-45 with a history of irregular fever and pain over the precordium of three months duration. There was no history of tuberculosis or rheumatic infection in the family. The disease started with headache, cold and cough which lasted for about ten days. Later, fever appeared with precordial pain and arthritis of the knee and ankle joints. Physical examination showed a moderately nourished individual without any evidence of anaemia, jaundice, cyanosis, clubbing of the fingers or oedema anywhere in the body. The knee and ankle joints were slightly tender but there was no effusion. Heart—The apex beat was neither visible nor palpable. Left border was in the midclavicular line. Heart sounds were faint over the mitral area and a well-marked pericardial rub was heard over the base of the heart reaching down to the level of the tricuspid area masking the normal heart sounds in those areas. Other systems were normal. Blood pressure was 110/70. Urine was normal. Blood showed W B C 8000 per cumm. Polymorph 80 per cent, Lymphos 18 per cent and Eos 2 per cent.

Radiological examination of the heart on 5-2-45 (fig 1) showed increase in the transverse diameter and a second picture (fig 2) taken with the head low showed increase in the basal shadow indicating pericardial effusion. Right transverse diameter 25 inches, left transverse 39 inches. Total transverse diameter 64 inches. Internal diameter of the chest 94 inches.

The patient was treated with rest in bed and salicylates by mouth. Examination on 8-2-45 showed that heart sounds were better heard and only a faint rub could be heard which lasted for another two days. Definite reduction of the size of the heart could be made out by percussion and the rub completely disappeared. Skiagrams taken on 24-2-45 showed absorption of the pericardial fluid. Right transverse diameter 18 inches, left transverse 31 inches. Total transverse diameter 49 inches. The patient was kept in the hospital for another two months under observation, there was no evidence of relapse of the condition and he was discharged cured on 6-4-45.

Case (2) Massive pericardial effusion absorbed by oral administration of salicylates and meersalyl injection—P R S, male aged 6 years, was admitted on 20-7-45 with a history of oedema and extreme dyspnoea of ten days duration. The complaint started with fever and pain over the left side of the chest three weeks ago. The doctor who examined him found pericardial rub in the left third and fourth intercostal spaces and signs over the left base of the lung.

Physical examination showed the child in a condition of extreme dyspnoea with general anasarca. Apex beat could be seen in the fourth intercostal space half an inch internal to the left mid-clavicular line. Left border extended to the midaxillary line, and the

right border, one inch external to the right lateral sternal line. Heart sounds were heard but were feeble and there were no murmurs. Jugular veins were abnormally dilated, and liver was enlarged up to the level of the umbilicus, pulsatile and tender. Lungs showed congestion of both the bases but more on the left. Blood pressure 80/56. Urine showed trace of albumin and motions showed nothing abnormal. A clinical diagnosis of pericardial effusion was made.

Radiological examination on 20-7-45 showed considerable increase in the cardiac shadow both to the right as well as to the left.

The child was put on sodium salicylate 45 grs., and Tr digitalis 20 ms a day. One injection of Mersalyl $\frac{1}{2}$ c.c. was given intramuscularly in addition. He gradually improved, oedema disappeared, liver was reduced and was only just palpable below the costal margin, heart considerably reduced in size and sounds could be clearly heard.

A second skiagram taken on 28-7-45 showed normal size of the heart. The child was discharged with instructions to continue the salicylates and digitalis and weekly injections of Mersalyl. The child is reported to be doing well and free from symptoms.

Case (3) Pericardial effusion gradually accumulated while in hospital—A P, female aged 15 years, was admitted on 27-4-43 with a history of fever and pain in the joints of 20 days duration.

Physical examination showed a poorly nourished individual without any oedema. Heart was enlarged, apex beat was one inch external from the left mid-clavicular line, right border just lateral to the right lateral sternal line. Systolic and presystolic murmurs were heard in the mitral area, and the systolic was conducted towards the axilla. Breath sounds were diminished over the left base. Liver and spleen were normal. She was running a low fever between 90°F and 102°F for nearly two months. The size of the cardiac dullness gradually increased, and heart sounds and murmurs which were heard before gradually became less audible. Urine showed a trace of albumin and a few leucocytes. Blood smear showed leucocytosis. Radiological examination on 25-5-43 (fig 3) showed considerable enlargement of the cardiac shadow and evidence of pericardial effusion. Right transverse diameter 3.1 inches, left transverse 4.3 inches, total transverse diameter 7.5 inches, and internal diameter of the chest 8.8 inches. Another skiagram taken with the head low showed increase in the basal shadow confirming the diagnosis of pericardial effusion. Aspiration was refused by the patient.

By rest and salicylates she gradually improved, temperature disappeared, cardiac dullness decreased in size, sounds were better heard and the patient was discharged relieved on 13-7-43. The patient died a few months later.

Case (4) Pericardial effusion, pleural effusion of the right side and death as a result of congestive heart failure—K S R, male aged 8 years, was admitted on 13-7-45 with a history of general anasarca, abdominal pain and dyspnoea of 2 months duration. The condition was worse for the last 3 days. He had a low irregular fever for 25 days, 2 years ago. Two months before the present com-

plaint, he had a similar attack Fifteen days before admission, the doctor who examined him outside, removed a small quantity of fluid from the right pleural cavity

Physical examination revealed a child with extreme dyspnoea, cyanosis, prominent jugular veins and general anasarca Heart apex beat was $\frac{1}{2}$ inch internal to the left mid-clavicular line Percussion note extended $\frac{1}{2}$ inch outside the left mid-clavicular line The right border of the heart could not be percussed out since the whole of the right axilla was dull Auscultation revealed feeble heart sounds Lungs showed dullness of the right base behind, breath sounds were feebly heard, and a few adventitious sounds were heard at the left base Liver was enlarged up to the level of the umbilicus and tender Urine showed trace of albumin and a few casts with occasional R B C Radiological examination of the heart on 11-6-45 showed enlargement of the cardiac shadow both towards the right and the left and in addition pleural haze of the right base Right transverse diameter 2 inches, left transverse 3 inches, total transverse diameter 5 inches, and total internal diameter of the chest 8.3 inches

The patient was treated with digitalis by mouth and injections of digitalin and mersalyl Aspiration was not attempted since the amount of fluid was not massive The condition became worse and the patient died of congestive heart failure on 15-7-45

Case (5) Rheumatic heart, pericardial effusion and congestive heart failure, fluid absorbed by salicylates by mouth and mersalyl injection—B N, female aged 25 years, was admitted on 5-7-46 with a history of dyspnoea and palpitation of one year's duration Physical examination showed enlarged area of cardiac dullness The whole of the left axilla was dull and the right border was 1 inch internal to the right mid-clavicular line Apex beat was lifted up in the 4th space 2 inches away from the mid-clavicular line Systolic and diastolic murmurs were heard at the apex Liver was enlarged and tender Fluoroscopy and radiological examination confirmed the diagnosis of pericardial effusion While in the hospital, cardiac irregularities were observed She was treated with mersalyl, digitalis and quinidine, and was discharged relieved with reduction in size of the heart This case will be dealt in detail in a separate communication

Case (6) Mitral stenosis and regurgitation with pericardial effusion confirmed by post mortem—T A, male aged 38 years, was admitted on 3-3-35 with signs and symptoms of congestive heart failure Physical examination showed cyanosis, prominent jugular veins, enlarged liver and oedema of the feet The apex beat was neither visible nor palpable, the left border was 2 inches external to the left mid-clavicular line and the right border half an inch external to the right lateral sternal line Auscultation showed roughening of the first sound with a faint diastolic murmur in the mitral, and reduplication of the second sound in the pulmonary areas Moist sounds were heard at both the bases of lungs Blood pressure was 104-74 Urine showed albumin, and a few hyaline,

epithelial and granular casts. Skiagram of the heart (fig 4) showed the triangular shadow typical of pericardial effusion. Measurements of the 'heart'—Right transverse 4.2 inches, left transverse 5.2 inches, total transverse diameter 8.7 inches. Total internal diameter of chest 11.0 inches. Blood urea was 51.74 mgs per 100 cc and blood Wassermann was negative.

The patient was treated with digitalis and diuretics by mouth and weekly injections of salyrgan. The patient gradually improved and the oedema completely disappeared. After a few days oedema reappeared and the symptoms of congestive heart failure became more pronounced. Blood pressure varied from 90 to 110 mm systolic and 60 to 80 mm diastolic. Repeated skiagram showed only the same picture of pericardial effusion. Aspiration of the fluid was not attempted. The patient gradually became worse and finally died on 14-5-35.

Postmortem was done on the same day. Pericardial cavity was distended with 20 oz of clear serous fluid, parietal pericardium was normal, but visceral pericardium showed numerous white fibrous patches scattered all over the surface. Heart weight 14 oz, right auricle was distended, right ventricle was hypertrophied, and the myocardium was pale and thickened. Mitral valve showed button-hole narrowing and a tendency to calcification, tricuspid orifice was dilated, but aortic and pulmonary valves were normal. Left auricle was dilated, left ventricular cavity was small and myocardium showed slight thickening. Both the pleural cavities contained serous fluid and lungs showed emphysema with hyperaemia. Liver, spleen and kidneys were enlarged and all showed passive congestion especially the liver.

2 *Myxoedema*

Case (7) K M, female aged 48 years, was admitted on 24-4-45 with a history of general weakness, anaemia and oedema of the body of one year's duration. Three years ago she had pains all over the body for which she took some indigenous medicines with some good effect. She was married, had no children and the periods were irregular for the last one year.

Physical examination showed a poorly nourished individual with anaemia, rough skin, scanty hair and solid oedema all over the body. Circulatory system: pulse was 60 per minute, apex beat was neither visible nor palpable, left border was in the mid-axillary line and right border just external to the right lateral sternal line. Pulmonary area was dull. Heart sounds were feeble in all areas and there was no pericardial rub anywhere. Blood pressure 114/94. Liver was palpable 2 inches below the costal margin, and spleen was normal. Except for the low intelligence there was nothing abnormal in the nervous system. Blood R B C 1.12 millions, W B C 11,600, Poly 62 per cent, Lymph 20 per cent, Mono 8 per cent and Eos 10 per cent. Smear showed anisocytosis, poikilocytosis and picture of microcytic anaemia. Basal metabolism—38.5 per cent. Blood cholesterol 211.6 mgs per 100 cc. Blood Wassermann strong positive. Urine nil abnormal.

Radiological examination of the heart on 19-5-45 (fig 5) showed increase in the cardiac shadow more towards the left and pulmonary conus was prominent. Right transverse diameter 19 inches, left transverse diameter 45 inches, total transverse diameter 64 inches, and internal diameter of the chest 92 inches. Another skiagram taken one month later on 18-6-45 showed exactly similar picture.

Pericardium was tapped on 18-6-45 in the fifth intercostal space in the midclavicular line, 11 oz of clear serous fluid was drawn and 150 c.c. of air was put in. Radiogram taken after paracentesis and introduction of air showed that 'heart' shadow was reduced in size, a small quantity of air was visualised in the pericardium, and the prominent pulmonary conus that was visualised in the previous picture has disappeared. Examination of the fluid showed proteins 170 mgs, and cholesterol 118 mgs per 100 c.c. The fluid showed only a few lymphocytes and was sterile on culture.

The fluid reaccumulated and on 28-6-45, 11 ozs of fluid was aspirated and 1000 c.c. of air was put in. This time a pneumothorax was produced accidentally causing displacement of the heart to the right. Skiagram on 10-7-45 (fig 6) showed partial absorption of air. Fluid at this time was thicker and contained 66 mgs of proteins, cells were more and consisted mainly of R B C and a few leucocytes.

Blood examination on 30-6-45 showed R B C 293 millions, and haemoglobin 55 per cent. Smear showed the picture of microcytic anaemia. She had ferri et ammonium citras for the anaemia. Thyroid extract was not given since it was not available.

The pneumothorax completely disappeared and fluid again began to collect in the pericardial cavity. The patient did not permit any more tapping and was discharged on 25-7-45. She could not be followed further.

3 *Congenital polycystic disease of the kidneys*

Case (S) V V, female aged 49 years, was admitted on 23-2-43 with a history of dyspnoea of two months duration. There was no history pertaining to the genito-urinary tract.

Physical examination showed a poorly nourished woman with anaemia, bad pyorrhoea and immature cataract of both eyes. Abdomen showed bilateral polycystic kidneys, right bigger than the left, and an enlarged liver palpable three fingers below the costal margin. Apex beat was neither visible nor palpable. Left border was 3 inches external to the left midclavicular line and the right border in the right midclavicular line. Heart sounds were feeble. Lungs showed congestion of the left base. Nervous system was normal. Blood pressure 145/110. Urine specific gravity 1010, albumin present in traces, bile and sugar absent. Centrifuged specimen showed only a few epithelial cells but no casts. Blood R B C 29 millions. Smear showed the picture of microcytic anaemia.

Radiological examination on 25-2-43 showed increase in the cardiac shadow both towards the left as well as to the right suggesting pericardial effusion. This was confirmed by other pictures taken with the head low. A tomographic picture (fig 10) also

showed pericardial effusion Right transverse diameter 33 inches, left transverse diameter 44 inches, total transverse diameter 77 inches, and internal diameter of the chest 10.2 inches Blood urea 35 mgs per 100 cc Uric acid 44 mgs Standard clearance 20.5 per cent Blood Wassermann negative Pyelogram on 10-3-43 showed the picture of polycystic kidneys Uterus and adnexia were normal

Pericardium was tapped by Dr R. Mahadevan on 9-3-43 by the epigastric route and 20 ozs of blood stained fluid was drawn The patient appeared better for a few days but became worse again and was discharged on 1-4-43 She could not be followed further

4 Unknown causation

Case (9) Massive effusion of the pericardium, removal of fluid and replacement by air produced considerable reduction in size of the pericardial cavity A small amount of fluid was still present at the time of discharge—T.L.N., male aged 50 years, was admitted on 5-3-45 with a history of cough, dyspnoea and epigastric pain of one month's duration He was married and had no children The complaint started two months before admission with fever for one week and pain over the chest more marked over the left scapular region

Physical examination showed a fairly nourished individual with extreme dyspnoea cyanosis, prominent jugular veins, and oedema of the feet Circulatory system pulse 100 per minute Left side of the chest was more prominent and apex beat was neither visible nor palpable Percussion showed that the whole of the left axilla was dull, and the right border was just external to the right mid-clavicular line Heart sounds were feeble, and no murmurs were heard Pericardial rub was carefully looked for and was absent Respiratory system—The whole of the left base showed congestion but no definite area of consolidation Liver was enlarged 2 inches below the costal margin and spleen was normal Both eyes showed immature cataract Blood pressure was 120/94 Blood R B C 4 millions, W B C 20,000 Poly 65 per cent, Lymph 30 per cent, Mono 1 per cent, and Eos 4 per cent Smear showed slight anisocytosis and poikilocytosis, and picture of microcytic anaemia Blood Wassermann negative

A clinical diagnosis of massive effusion into the pericardium was made Radiological examination on 5-3-45 (fig 7) confirmed the clinical diagnosis

Pericardium was tapped on 7-3-45 in the fourth intercostal space $\frac{1}{2}$ inch to the left of the sternum and 10 oz of serous fluid was drawn, and 300 cc of air was put in Skiagram showed the presence of a small quantity of air in the pericardial cavity with a horizontal level of the fluid Examination of the fluid showed 500 mgs of proteins per 100 cc and only few leucocytes Culture was sterile Blood pressure after tapping was 110/70

Electrocardiogram taken on 10-3-45 showed sinus tachycardia and low voltage in all the leads P was normal in Leads I and II flat in Lead III and indistinct in Lead IV F P-R 0.12 seconds, T positive in Lead I, flat in Leads II and III and biphasic in Lead IV There was no alteration in S-T segment

Pericardium was again aspirated on 10-3-45 in the fifth intercostal space in the left midclavicular line and 55 ozs of serous fluid was drawn, and 750 cc of air was put in. Percussion showed tympanitic note over the precordium, and radiological examination showed reduction of the size of the pericardial cavity, horizontal level of the fluid and the outline of the heart (fig 8). There was no evidence of prominent pulmonary conus or left auricular enlargement to suggest mitral stenosis. The dyspnoea was completely relieved and the patient was able to walk about.

A week later (16-3-45) examination showed that the left axilla was dull, the base was hyperresonant, and pericardial rub could be heard in the third and fourth intercostal space just to the left of the sternum. Radiological examination on 17-3-45 showed that a major portion of the air had been absorbed and fluid had reaccumulated. Fourteen ounces of fluid was aspirated and 750 cc of air was put in. The fluid at this time was thicker and contained 2,800 mgs of proteins per 100 cc. R B Cs also were seen in addition, and culture was sterile. One week later (23-3-45) radiological examination showed that air completely disappeared and fluid had collected again. Three days later a perineal abscess developed and it was controlled by sulphathiazol and drainage. Examination a month later (23-4-45) showed considerable reduction in size (fig 9) and heart sounds were clearly heard.

Electrocardiogram taken on 28-4-45 showed sinus tachycardia (120 per minute). The amplitude of all the waves were increased in all the leads, T was biphasic in Leads III and IV F. There was no alteration in S-T segment.

The patient was discharged practically cured on 28-4-45.

Case (10) Haemorrhagic effusion of unknown causation —M G, male aged 25 years, was admitted on 17-8-44 with a history of dyspnoea and discomfort in the upper abdomen of 4 months duration. The patient was married and had 3 children, all healthy, and was quite healthy before the symptoms started. The complaint started with nausea and vague discomfort in the abdomen and dyspnoea developed soon after. He was treated outside with some indigenous drugs, got worse and was finally admitted in the King George Hospital.

Physical examination showed a poorly nourished individual with anaemia, dyspnoea, prominent jugular veins and oedema of the feet. There was no cyanosis. Circulatory system: the precordium was bulging and apex beat was neither visible nor palpable. Percussion showed the left border $1\frac{1}{2}$ inches external to the mid-clavicular line and the right border 1 inch external to the right lateral sternal line. Auscultation revealed only feeble heart sounds and there were no murmurs. There was no evidence of pericardial rub. Pulse was 86 and pulsus paradoxus was present. Blood pressure 130/90. Liver was enlarged up to 3 fingers below the costal margin and tender. Spleen was not enlarged. Lungs showed a few moist sounds at the left base.

Clinical diagnosis of pericardial effusion was made. Radiological examination on 18-8-44 showed increase in the size of the heart both to the right and left suggesting pericardial effusion. Right transverse diameter 35 inches, left transverse 52 inches, total transverse diameter 87 inches and internal diameter of the chest 106 inches.

On 19-8-44 the pericardium was tapped in the third left intercostal space just to the left of the sternum and 3 oz of haemorrhagic fluid was aspirated. While in hospital he had low irregular fever varying between 99° and 101°F. He was put on diuretics by mouth and injections of mercurial diuretics (Neptal). The patient improved to a certain extent and oedema was considerably reduced. He refused to remain any longer and so was discharged from hospital on 5-10-44. He could not be followed up further.

Case (11) Pericarditis with haemorrhagic effusion, patient admitted in a moribund condition, and died in the hospital, post-mortem showed fibrinous pericarditis with haemorrhagic effusion—M V, male 40 years old, was admitted on 30-11-43 with a history of dyspnoea, cyanosis and oedema of the legs of 15 days duration.

Physical examination showed enlargement of the 'heart', left border in the mid-axillary line, and right border 1 inch external to the right lateral sternal line. Heart sounds were feeble. There was no evidence of pericardial rub. Blood pressure 140/100 pulse was feeble. Liver was enlarged 3 fingers breadth below the costal margin and tender, and spleen was not palpable. Lungs showed moist sounds at both the bases. Radiological examination on 2-12-43 (fig 11) showed enlargement of the cardiac shadow, irregularity in the outline and evidence of pericardial effusion. Right transverse diameter 24 inches, left transverse 51 inches, total transverse diameter 75 inches, and internal diameter of the chest 105 inches. Urine was small in quantity and contained albumin and a few casts.

Pericardium was tapped on 2-12-43 in the fourth left intercostal space just to the left of the sternum and 3 oz of blood-stained fluid was drawn.

Electrocardiogram taken on 3-12-43 showed R S R 80 per minute, P-R interval 0.18 of a second, T faint in Lead I, biphasic in Lead II, flat in Lead III and very faint in Lead IV F, left axis deviation and low voltage in all the leads.

The patient gradually became worse and died on 4-12-43. Post-mortem was done on 7-12-43. Heart was considerably enlarged and pericardium contained 20 oz of blood-strained fluid. The visceral pericardium covering the heart was shaggy and bands of adhesions were observed between the parietal and visceral pericardium (fig 12). Lungs showed marked congestion, liver was enlarged and showed scattered abscesses over the surface containing greenish yellow pus. Spleen was enlarged. Kidneys were small, contracted and under microscope showed evidence of arteriosclerosis.

5 Non-inflammatory effusion

Case (12) Pericardial effusion associated with general anasarca and congestive heart failure—K. A., female aged 22 years, was admitted on 28-12-45 with dyspnoea and oedema of the whole body of one month's duration. Patient had a child one year ago and died 7 days after delivery.

Physical examination showed general anasarca, clubbing of the fingers, cyanosis and prominent jugular veins. Heart borders could not be made out by percussion since dullness extended far to the right and to the left. Apex beat was neither visible nor palpable, heart sounds were rapid and feeble and no murmurs were heard. Lungs showed diminished percussion note at both the bases and occasional moist sounds. The patient showed slight improvement after digitals and diuretics.

Radiological examination on 29-12-45 showed enlargement of the cardiac shadow both towards the right and left suggestive of pericardial effusion.

On 31-12-45 the patient became extremely dyspnoeic, oedema of the legs diminished but oedema of the face and neck became more prominent. The apex beat was felt $1\frac{1}{2}$ inches distal to the mid-clavicular line. Heart sounds were feeble and gallop rhythm was present. Blood pressure was very low, 20 systolic and diastolic could not be estimated. Profuse diuresis occurred after mercuryl injection (200 oz in 24 hours), oedema was reduced and a definite systolic murmur could be heard at the apex. On 3-1-46 the face again became swollen, quantity of urine diminished, pulse became rapid and feeble, and blood pressure rose up to 70 systolic but diastolic could not be made out.

The patient gradually became worse and died at 8 p.m. on 3-1-46. Post mortem done on 5-1-46 showed 3 pints of fluid in the peritoneum, 12 oz of straw coloured fluid in the pericardium, haemorrhagic broncho-pneumonia of the lungs, enlarged and flabby heart, passive congestion of the liver and granular kidneys.

ÆTIOLOGY

Age and sex—There were 8 males and 4 females. Two cases occurred in children. The minimum age was 6 and the maximum 50 years.

Rheumatic infection—Six cases belonged to the rheumatic group, one showed a small quantity of fluid, and another massive effusion. The other 4 showed only a moderate amount of effusion. In case No. 6 the clinical diagnosis was not definite, but radiological appearances suggested pericardial effusion and postmortem showed 20 oz of serofibrinous fluid in addition to mitral stenosis. Smith and Williams (1932) found 8 cases of rheumatic infection in a series of 113 cases (7.1 per cent) and consisted of 3 cases of mitral stenosis, 3 of aortic insufficiency, 1 of aortic insufficiency and mitral stenosis, and 1 of mitral stenosis with tricuspid insufficiency. In the present series, only 3 cases showed involvement of the mitral valve (stenosis and regurgitation), and in the other 3 only myocarditis was present in addition to effusion. Levine considers that effusion develops in

most cases of rheumatic pericarditis but might vary in quantity. Rheumatic pericardial effusion is seen more often in New England than in South lower (White). Of the 13 cases of massive pericardial effusion of Fenichel and Epstein, 6 were rheumatic in origin.

Myxoedema and pericardial effusion—Zondek (1920) reported watery imbibition of myocardium in myxoedema. Goldberg (1927) found pericardial effusion in 7 out of 22 sheep made myxoedematous by removal of the thyroid gland. Gordon (1920), Freeman (1934), Huxthal (1935) and Kunitz (1936) observed larger effusions. In case No. 7 the patient had no symptoms at all of effusion. Basal metabolism was -38.5 per cent and blood cholesterol 211.6 mg per 100 c.c. In all 22 oz of serous fluid was aspirated. 11 oz of fluid was drawn in the first instance and another 11 oz at the end of another week. The protein content was only 170 mg per 100 c.c. and the cholesterol content of the fluid was low 118 mg.

Tuberculous pericarditis—In massive effusions requiring repeated pleural tapping, tuberculosis is to be suspected. The fluid is usually sterile on culture but guinea pig inoculation may settle the diagnosis (Levine). Isolation of tubercle bacilli from pericardial effusion is difficult and if the culture is positive, the prognosis is grave (Harvey and Whitehill). Cases are reported by Suzman, Seilars, Barret and Coie, Parkinson and Ellman in which bacillus could not be detected from the aspirated fluid, but on postmortem examination, they were found to be tuberculous in origin. Keefer (1937) found large effusions in 7 cases from a series of 20 cases of tuberculous pericarditis. Patel (1942) reported 5 cases of pericardial effusion of which he thinks 3 were tuberculous, although no tubercle bacilli were seen in all the haemorrhagic effusions. Case No. 9 of the present series showed massive effusion in the pericardium. The fluid was sterile on culture and there were no tubercle bacilli. Seventy-nine ounces of fluid were drawn, ten in the first, fifty five in the second and fourteen in the third, within an interval of ten days. The fluid in the first instance was sero-fibrinous and contained 0.5 per cent proteins, in the 2nd instance it was thicker and contained 2.8 proteins and at the last exploration, the fluid was haemorrhagic. It is quite possible that this case might be tuberculous in origin although tubercle bacilli were not isolated.

Haemorrhagic effusion—Three of these cases showed haemorrhagic effusion of which one was associated with congenital polycystic disease of the kidneys. In that case the blood pressure was high but the blood urea was not increased. In the other two cases, no cause could be found and in the last case (No. 11), the patient was admitted in a moribund condition, the blood pressure was slightly raised ($140/100$) and electrocardiogram showed gross myocardial damage. The patient died and postmortem showed fibrinous pericarditis (fig. 12) without any evidence of tuberculosis either to naked eye or under the microscope. The kidneys were small and contracted and showed evidence of arteriosclerosis under the microscope.

Malignant pericardial effusion—Smith and Williams (loc cit) found only 4 cases of neoplastic invasion of the pericardium, but

none of these were associated with effusion. Majority of the tumours of the pericardium are secondary. Haemorrhagic effusions suggest malignancy. Large quantities of fluid may be present when there are no adhesions and presence of malignant cells in the fluid confirms the diagnosis (King).

Coronary thrombosis and pericardial effusion—The condition is extremely rare. Levine (1929) observed only one case (No 64) in a series of 145 cases of coronary thrombosis. The diagnosis was not suspected during life but postmortem showed 1000 cc of fluid in the pericardial cavity. Schwaitz (1934) reported pericardial effusion in a man of 50 following coronary thrombosis and who completely recovered after removal of the fluid. In pericardial effusion associated coronary occlusion was found in 2 cases by Camp and White (1932) and in another 2 by Smith and Williams (1932). Master and Jaffe (1935) reported 2 cases of effusion observed by them during a period of 6 months. Nichol (1938) reported a case of massive pericardial effusion complicating acute coronary thrombosis from which 500 cc of fluid was removed.

Hydro-pneumo-pericardium—Lyons (1938) reported a case of tuberculous pericardial effusion from which 2,200 cc of fluid was removed. A few days later he developed extreme dyspnoea which was clinically thought to be spontaneous pneumothorax, proved to be one of hydro-pneumo-pericardium by radiological examination.

Non-inflammatory effusion—In case No 12, the patient showed non-inflammatory effusion of the pericardium in association with effusion in the peritoneum. Blood pressure in this case was normal in the beginning but on the day of death it was 20 systolic and 0 diastolic. Postmortem showed granular contracted kidneys. Modi (1942) described 2 cases of pericardial effusion, the first one due to anaemia and the second due to syphilitic involvement of the heart.

Purulent pericarditis was not present in the present series. Smith and Williams (loc cit) in a series of 113 cases, found 17 cases and in 74 per cent of these intra-thoracic suppuration was the primary cause. Shipley and Winslow (1935) from a review of the literature found 99 cases and reported 5 more cases. Patel (1942) described 2 cases of purulent effusion, both were cases of amoebic abscess of the liver rupturing into the pericardial cavity.

DIAGNOSIS

Clinical diagnosis of pericardial effusion is made more often now than before and in massive effusions the diagnosis is easy. Pain, dyspnoea, cough and occasionally cyanosis may be present and when the effusion is massive as in Case (6), dyspnoea may be extreme. In the earlier stages when only small quantity of fluid is present as in Case (2), fever, increased area of cardiac dullness and pericardial rub confirm the diagnosis. If the area of cardiac dullness increases with feeble heart sounds and pericardial rub at the base, the diagnosis is definite. As the effusion increases the physical signs become much more evident, precordium bulges as in (case 8), area of cardiac dullness increases both towards the right and left, the shape of dullness sometimes assumes a triangular shape, the apex beat is within

the area of cardiac dullness, heart sounds become feeble and pericardial rub might or might not be heard, and if present confirms the diagnosis. Increase in the area of cardiac dullness at the base in the recumbent position especially when the head is low, may be taken as diagnostic of pericardial effusion.

Ewart (1896) described 10 physical signs of pericardial effusion of which the 8th and 10th signs put together constitute Ewart's sign. This is sometimes called "Bamberger's sign". The 8th sign consists in a square shaped area of dullness at the base of the left lung behind, extending from the spine to the scapula and ending in a vertical border. The horizontal line of dullness above, does not go above the 10th rib and in some cases the right border goes to the right of the middle line and in massive effusion the line of dullness extends far to the right. When the diagnosis is doubtful by the physical signs in front of the chest, this sign confirms the diagnosis of pericardial effusion. The 10th sign consists in a patch of tubular breathing and aegophony 2 inches in diameter just below the inferior angle of the left scapula and is produced by collapse of the lung caused by the pressure on the bronchus by pericardial effusion. Levine and Gevalt (1940) suggested rheumatic infection of the lung by extension from the heart as the cause of this pulmonary lesion.

Levine considers the increase in the area of cardiac dullness from day to day is much more significant than that of enlargement observed on a single day. Obtuse cardio-hepatic angle (Rotch's sign) which was originally thought to be diagnostic of pericardial effusion has lost its value since massive effusions have been observed in cases where this sign was absent.

In the case of a boy aged 6 years, the blood pressure was 80/56. In two other cases in which the kidneys were involved, it was 145/110 in polycystic disease of the kidney, and in another, 140/100. There was no appreciable change in the other cases and the blood pressure varied from 104 to 130 systolic and 70 to 94 diastolic.

Smith and Williams (1932) from a study of blood pressure in 23 cases in which fluid exceeded 150 cc, found the average systolic 121.8 mm and diastolic 70.2 mm with a pulse pressure of 51.6 mm. In small effusions up to 200 cc, it was 134.5 systolic and 67.8 diastolic, and in large effusions from 700 to 750 cc, systolic was 103.5 and diastolic 59 mm. Pulsus paradoxus may be present and was found only in one case (No. 10) of the present series.

Beck (1935) described three characteristic features of massive pericardial effusion: (1) low arterial pressure, (2) high venous pressure, and (3) a quiet or a small heart. In case (8) of the present series that showed massive pericardial effusion, the blood pressure and 120/94 and came down to 110/70 after the removal of the effusion. The pulse rate in this case varied from 90 to 100 per minute and the size of the heart (fig. 8) was neither big nor small.

Diagnosis from a dilated heart is sometimes difficult, especially when the apex beat cannot be palpated and when the heart sounds are feeble. Gross myocardial damage is one of the conditions that gives greatest difficulty in diagnosis. Difficulty is also felt in cases

of myxoedema In case (7), the diagnosis was easy because the heart sounds were not heard and the whole of the left axilla was dull Recently another case of myxoedema was admitted with a huge heart and the heart sounds were feeble, but the apex beat could be felt far out the mid-clavicular line which lead to the correct diagnosis of dilated heart When pericardial effusion is associated with congestive heart failure and pleural effusion, diagnosis becomes difficult In case (4), the effusion was on the right side and the diagnosis was simple Fenichel and Epstein (1946) reported a case diagnosed as pleural effusion, in which fluid was aspirated and air was introduced The radiological examination showed hydro-pneumo-pericardium showing that the original condition was only massive effusion of the pericardium and the enlargement of the area of cardiac dullness to the right was mistaken for displacement of the heart by a massive left sided pleural effusion

Radiological diagnosis—Roesler (loc cit) observed that only effusions above 250 cc could be detected radiologically Fluoroscopy shows enlargement of the cardiac shadow The contractions are feeble and it is not possible to distinguish the individual contractions of the chambers of the heart Indistinct wave-like movements are seen occasionally on the outer margin of the shadow (Levine) Straightening of the left border has been observed A pear shaped outline is seen in moderate effusion as in case (6) (fig 4) and change in the shape of the heart occurs in the recumbent posture especially when the head is in lower position, case (1) (figs 1 and 2) and case (3) Smith and Williams (loc cit) were able to find only 5 cases in a series of 34 cases in which radiological appearances suggested pericardial effusion

The radiological appearances seen in the 12 cases are given in a tabular form—Table 1, on page 141

In case (1) transverse diameter of the heart was increased and a skiagram taken with the head low showed increase in the basal shadow (fig 2) A second picture showed considerable reduction in the size as fluid was absorbed A picture taken on the same day with the head low showed no increase in the basal shadow In case (2) the first skiagram showed considerable increase in the size both towards the right and left A second picture showed considerable reduction in the size, and the heart has regained normal size In this case the clinical evidence was more definite of pericardial effusion because the apex beat was far inside the outer border of the cardiac dullness In case (3) the 'heart' shadow occupies practically the whole of the chest (fig 3) Another picture taken with the head low showed increase in the basal shadow In case (4) a skiagram taken before the patient was admitted showed pleural effusion in addition to the increase in the "heart" shadow A second picture could not be taken since the condition of the patient was very bad Clinical examination showed that the left border was 1 inch external to the mid-clavicular line and the apex beat was well within the left border In case (5) the apex beat was lifted up, which was supposed to be a characteristic feature of pericardial

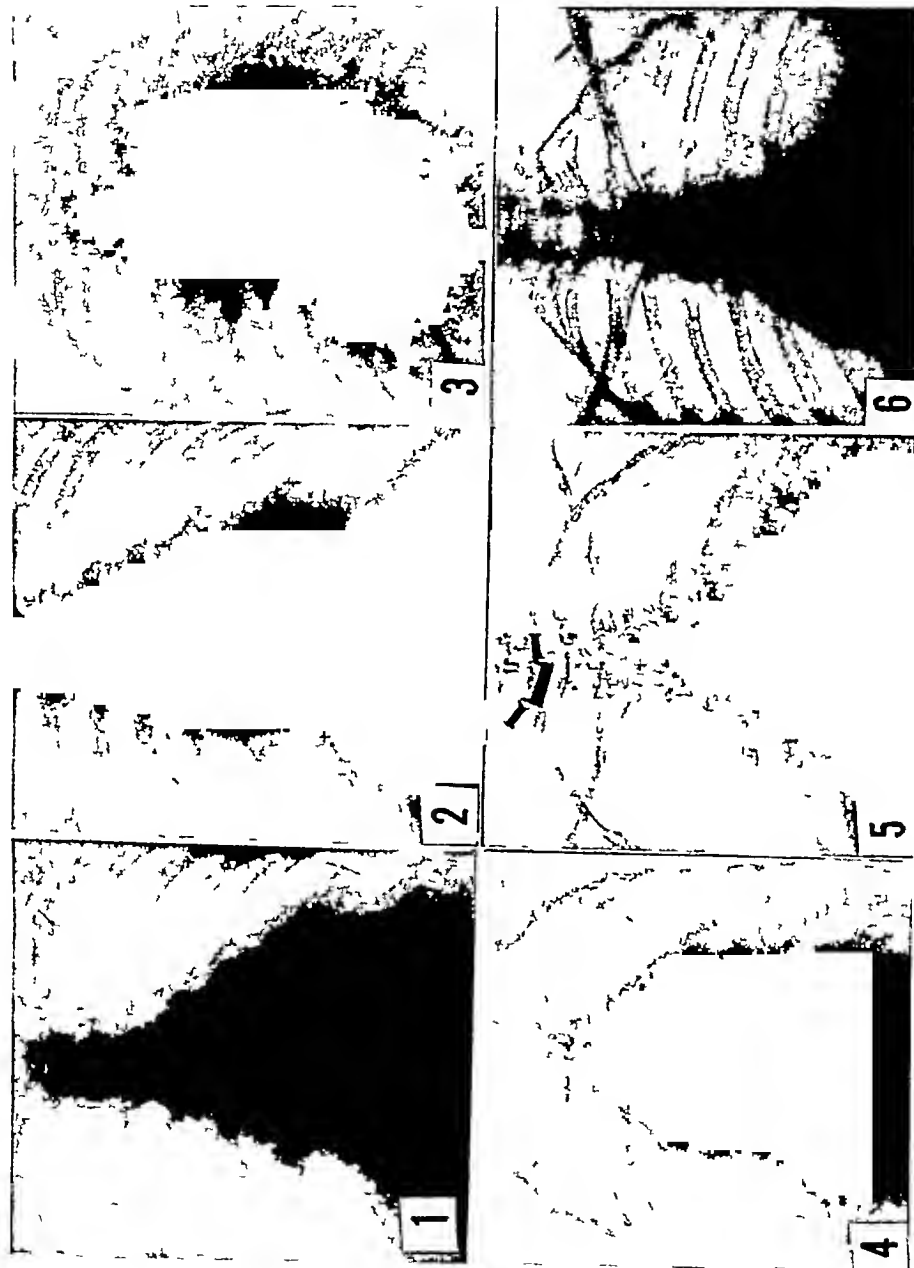


Fig (1) Case (1) taken on 5-2-45 Rheumatoid pericardial effusion showing enlargement in the size of the heart
 Fig (2) Case (1) taken on the same date a few minutes later with the head low showing increase in the shadow at the base of the heart and the downward displacement of the fluid with change of position
 Fig (3) Case (3) taken on 25-5-45 Rheumatoid infection showing massive pericardial effusion double mitral in addition
 Fig (4) Case (6) taken on 20-3-35 Rheumatoid infection showing the triangular shadow double mitral in addition
 were seen at postmortem
 Fig (5) Case (7) taken on 19-5-45 Myxoedema with effusion showing prominent pulmonary conus
 Fig (6) Same case as above taken on 10-7-45 The fluid was removed and air was introduced This produced a pneumothorax and displaced



Fig (7) Case (9) taken on 3.7.45. Same case as above taken on 10.2.45 from which 63 oz of fluid has been drawn and 1030 cc of air has been put in showing the heart shadow is normal. The heart shadow is irregular and considerably enlarged. Three ounces of blood stained effusion was withdrawn and postmortem showed 20 oz of haemorrhagic fluid. Congenital poly cystic disease of the kidney. Twenty ounces of haemorrhagic fluid. Fig (8) Case (8) taken on 27.4.45. The fluid has been practically absorbed. Fig (9) Case (10) taken on 25.2.45. The fluid has been practically absorbed. Fig (10) Case (11) taken on 2.12.45. Haemorrhagic effusion of unknown causation. The heart shadow is irregular and considerably enlarged. Fig (11) Case (12) The postmortem specimen of case No 11 showing the pericarditis.

Table 1

Case No	Date	Rt trans diameter (inches)	Lt trans diameter (inches)	Total trans diameter	Trans diameter of chest	Remarks
Rheumatic infection.						
(1)	5-2-45 (Fig 1)	2.5	3.9	0.4	0.4	Fluid absorbed
	24-2-45	1.8	3.1	4.0	0.4	Massive effusion globular shadow
(2)	20-7-45					Massive effusion
(3)	25-5-48 (Fig 3)	3.1	4.3	7.4	8.8	Congestive heart failure with
(4)	11-6-45	2.0	3.0	5.0	8.3	pleural effusion
(5)	5-7-40	3.3	4.6	7.9	9.6	Definite reduction in size
	25-7-40	2.9	4.7	7.0	9.5	
	31-12-40	2.9	4.6	7.5	9.7	
(6)	20-3-45 (Fig 4)	4.2	5.2	9.4	11.0	Confirmed by P M 20 oz of fluid
Myxoedema						
(7)	19-5-45 (Fig 5)	1.9	4.5	0.4	0.2	Shadow considerably enlarged
	18-6-45	1.9	4.5	0.4	0.2	Prominent pulmonary conge
	26-6-45	2.5	3.0	0.4	0.2	Ten ounces of fluid were withdrawn
	10-7-45 (Fig 6)					and air put in
	20-7-45	2.3	4.0	0.3	0.2	Fluid has reaccumulated
						Pneumothorax left heart dis
						placed to the right
						Fluid has reaccumulated
Congenital polycystic disease of the kidney						
(8)	25-2-43 (Fig 10)	8.3	4.4	7.7	10.2	Tomographic picture Twenty oz of haemorrhagic fluid withdrawn
Unknown causation—Massive effusion						
(9)	5-3-45 (Fig 7)	4.15	4.7	8.85	9.9	Massive effusion
	7-3-45	"	"	"	"	Ten oz of fluid were withdrawn and 800 c.c. air put in
	17-3-45 (Fig 8)	3.1	4.5	7.0	"	Fluid and air
Size of the heart inside the pericardial cavity	10-3-45	1.6	3.2	3.8	"	Major portion of air absorbed (Fluid and air)
	17-3-45	3.45	4.5	7.95	"	
	23-3-45	8.0	4.05	7.05	"	After removal of 14 oz of fluid
	23-4-45 (Fig 9)	3.7	4.3	8.0	"	Fluid has reaccumulated no air
		2.25	3.8	0.05		Fluid practically absorbed
Haemorrhagic effusion.						
(10)	18-8-44	3.5	5.2	8.7	10.6	Three oz of haemorrhagic fluid withdrawn
(11)	2-12-43 (Fig 11)	2.4	5.1	7.5	10.5	Three oz of bloodstained fluid aspirated P M 20 oz of blood stained fluid
Non-inflammatory effusion						
(12)	20-12-45					Triangular shadow typical of effusion

effusion. Subsequent pictures showed reduction in the size. In case (6) the shadow was of a triangular shape, typical of pericardial effusion (fig 4). This was confirmed by postmortem and 20 oz of sero-fibrinous fluid was found in the pericardial cavity.

In case (7) the first picture showed increase in the "heart" shadow both towards the right and left, but the important feature was the prominent pulmonary conus (fig 5). Ten ounces of fluid were drawn and air put in. Pulmonary conus had disappeared and the air was visualised in the pericardial cavity. A subsequent picture showed reaccumulation of the fluid, 11 oz of fluid were again drawn and 1,000 c.c. of air was put in. This unfortunately produced a pneumothorax and the heart was displaced towards the right (fig 6). The subsequent pictures taken showed that the air was

absorbed, partial collapse of the lung was present and a photograph taken just before discharge showed complete disappearance of the air but still fluid has reaccumulated

In case (8) a series of skiagrams was taken, and all showed increase in the "heart" shadow. Figure (10) is a tomographic picture. Twenty ounces of haemorrhagic fluid were drawn by the epigastric route.

In case (9) the first radiogram showed that the "heart" shadow occupied the whole of the chest indicating massive effusion (fig 7). Withdrawal of 10 oz of serofibrinous fluid and introduction of 300 cc of air showed only a small quantity of air in the pericardial cavity. During the second aspiration 55 oz of fluid was drawn, and 750 cc of air was put in. The picture (fig 8) is typical of hydro-pneumopericardium showing the horizontal level of the fluid. Subsequently some more fluid was removed. Fluid reaccumulated, and it had to be removed again. Fig 9 shows that the shadow has regained the normal size and the fluid was practically absorbed.

In case (10) the skiagram showed the definite outline of the pericardium with increase in the transverse diameter, and 3 oz of haemorrhagic fluid were withdrawn. In case (11), the "heart" size was increased, irregular in outline (fig 11) and 3 oz of blood-stained fluid was aspirated. Patient died two days later. Postmortem showed 20 oz of blood-stained fluid.

In case (12) a triangular shadow was seen showing the typical shadow of pericardial effusion. The patient died and on postmortem 12 oz of serous fluid was observed in the pericardial cavity.

Freedman (1937) reported two cases of encapsulated pericardial effusion in which the condition had to be differentiated between mediastinal tumour and aneurysm. This is usually seen on the right side and fluoroscopy shows that the shadow becomes elongated during inspiration and broadened during expiration. Aspiration of the fluid and introduction of air confirms the diagnosis, showing that the encapsulated cavity is in communication with the pericardial cavity.

Kymography—Berner (1937) observed vigorous pulsation of the aortic knob and poor pulsations of the left ventricle, and the pulsations of the aorta and left ventricle became equal after the absorption or removal of the fluid. Sellors (1944) found kymography to be of considerable value in the diagnosis in one of his cases. Fenichen and Epstein (1946) observed small amplitude of pulsation of the heart and blood vessels. This was not done in any of our cases.

Electrocardiography—Electrocardiograms were taken only in 3 of the present series. One case of massive effusion (case 9) showed sinus tachycardia, small P in Lead III, low amplitude of T, and low voltage in all Leads. There was no alteration in S-T segment. A second electrocardiogram taken after the removal of the fluid showed increase in the amplitude of all the waves showing the effect of removal of the effusion. The second case (case 11) showed regular sinus rhythm, normal P-R interval, low amplitude of T, and low voltage in all Leads. There was no alteration in the S-T segment.

A second electrocardiogram could not be taken since the patient died a few days after admission. In the 3rd case (case 3) electrocardiogram showed all cardiac irregularities and auriculo-ventricular dissociation but all these changes were due to associated rheumatic infection of the myocardium. This case, as mentioned earlier, will be published in detail in a separate communication.

Oppenheimer and Mann (1923) reported decreased voltage in 7 cases of pericardial effusion. Gager (1924) observed in addition to low voltage, disturbance in P-R interval and change in RS-T segment with paradoxical relationship in Leads I and III and abnormalities in Q and T. These changes disappeared after the removal of the fluid. Wood and White (1925) in a case with terminal pericardial effusion found elevation of RS-T segment in Leads I and II and slight deviation in Lead III and thought that these changes were due to uraemic condition of the patient. Similar changes were observed by Scherf (1927), and Scott et al (1929). Agostini and Papp (1927) observed auriculoventricular and bundle branch block in two cases of rheumatic pericardial effusion. Schwab and Herrmann (1935) from a study of electrocardiographic changes found decrease in voltage in QRS, elevation of RS-T segment, and progressive changes in the T following absorption of fluid in 7 cases of which 6 showed pericardial effusion.

Tung (1941) found Q-T interval normal in massive pericardial effusions, but prolonged in marked enlargement of the heart, and this fact could be utilised to distinguish between the two conditions.

Pardee (1942) found low voltage of T and QRS in massive effusions.

Vakil (1942) made an exhaustive study of electrocardiographic changes in pericardial effusions and reported the changes observed by him in 28 cases. He found low amplitude, low voltage in all Leads, normal duration of the waves, tendency to prolongation of the P-R interval, tendency to notching of the QRS in 21.4 per cent of the cases and changes in the RS-T segment in 43 per cent of the cases, auricular fibrillation in one case, and complete heart block in another.

White (1944) found in acute pericarditis with effusion, changes in the T wave, alteration of the S-T segment and low voltage in all Leads. Although elevation of the S-T segment simulated coronary occlusion, they had the same direction in all the Leads, and Q was not present at all.

The low voltage occurring in the pericardial effusion is due to the short-circuiting action of the currents by the fluid which surrounds the heart, and the same phenomenon has been observed in experimental animals when saline was injected into the pericardial cavity. The low voltage comes back to normal when the fluid is removed. When there are adhesions between the heart and the pericardium in addition to the fluid, the low voltage may not be usually found. The low voltage was observed in 3 cases of myxoedema with pericardial effusion and the similarity of electrocardiogram in myxo-

dema and pericardial effusion could be attributed only to the presence of fluid in the pericardium (Scherf and Boyd)

Aspiration of the fluid—The final diagnosis of pericardial effusion consists in the demonstration of fluid on aspiration. Different methods of approach to the pericardium have been suggested (1) in the 3rd, 4th, 5th or the 6th intercostal space just to the left of the sternum, (2) in the 5th intercostal space just to the right of the sternum (3) between the apex and the left border in the 5th intercostal space, (4) the epigastric route, and lastly (5) just below the inferior angle of the left scapula (King). A 20 c.c. syringe with a big exploring needle is all that is necessary. The patient is first placed in the semi-recumbent posture. The area to be punctured is first infiltrated with novocaine and then the exploring needle is introduced. After the first $\frac{3}{4}$ of an inch, the piston is to be drawn and if no fluid comes out the needle is pushed further and the piston is drawn again and this process is repeated till the fluid is drawn into the syringe. In massive effusions there is no danger of puncturing the heart, but in smaller effusions, if the needle is pushed too far, it might lacerate the surface of the heart. It is very easy to find out when the needle touches the heart, as the contractions of the heart can be felt by the needle and when this happens the needle should immediately be withdrawn. In the four cases, No 7, 9, 10 and 11, the exploration was first done in the 4th left intercostal space just to the left of the sternum. When the fluid is small in quantity or when some fluid has already been removed as in cases 7 and 9, the site chosen should be the one between the apex and the left border of the cardiac dullness. In case 8, the aspiration was done through the epigastric route. Removal of the fluid was not attempted in cases of rheumatic pericardial effusion, but in case 3 where aspiration was indicated, it was refused by the patient. In three other cases of myxoedema where a doubt arose, as to the presence of fluid, aspiration of the pericardium was done, but no fluid was withdrawn.

Left postero-thoracic route is usually used only when the fluid is not tapped by the other routes. White (1944) and Levine (1945) have drawn 500 c.c. of fluid by this route when all the other methods failed. According to Levine, the different procedures adopted is only a matter of custom and not because of the superiority of one method over the other. In case of doubt whether the fluid is in the pleura or in the pericardium as in the case of Fenichel and Epstein (loc cit) introduction of air and the demonstration of presence of air and fluid in the pericardial cavity will settle the diagnosis.

TREATMENT

Rheumatic infection—Effusions are usually small and are treated with salicylates 60 to 120 grains a day. This is sufficient when the drug is continued for about a fortnight as in case (1), but if the fluid is sufficiently large, mersalyl injections once a week have to be given in addition as in case (3). The fluid will be completely absorbed by this procedure. Herman (1929), Casoute et al (1934), and Pallard and Badenand (1937) reported successful results with

salicylates in the treatment of rheumatic pericardial effusions, whereas Murray Lyon was not able to find any beneficial results. Schultz (1931) found amidopyrine useful in the absorption of fluid. Boas and Ellenberg (1940) reported rapid reduction of fluid in two cases by administration of large doses of salicylates. In cases 1 and 3 of the present series, only 20 and 30 grains of salicylates were given in a day. Observations of Carvati and Cosgrove (1946) show that addition of smaller doses of sodium-bicarbonate to the mixture increase the concentration of salicylates in the blood and this method of administration can be better utilized in the treatment of rheumatic pericardial effusion.

Although Riolanus (1650) suggested paracentesis of the pericardium by the trans-sternal route, it was put in practice only a century later. Aspiration of the fluid in rheumatic infection is indicated only in massive effusions causing dyspnoea as in case (3). In this case, aspiration was refused by the patient and so it could not be done. In other conditions aspiration is indicated even in moderate effusions. Fall in blood pressure is an indication for paracentesis (Fishberg). The method of approach has already been described in the section on diagnosis. Sometimes, repeated aspirations have to be done as in cases 7 and 9, and in case 9, 79 oz of fluid was withdrawn in a short period of 10 days, and 55 oz of fluid was removed in one sitting. In some cases the fluid might stop after a few ounces are withdrawn, but a slight change in the direction of the needle is sufficient to get at the fluid again.

Aspiration of the fluid should not be undertaken lightly, since accidents have happened even in experienced hands. King (1944) has recorded the following complications—(1) shock, (2) injury to the internal mammary vessels, (3) puncture of the coronary vessels producing haemo-pericardium, (4) laceration of the heart, and (5) injury to the pleura and lung resulting in pleural effusion or pneumothorax. Levine has observed two cases with extensive pleural effusion within 48 hours after tapping the pericardial cavity and he thinks that the fluid was poured out into the pleural cavity through the rent left in the pericardium, and in these cases the pleural effusion had to be tapped. Fatality may occur and two cases were observed by Levine. Pneumo-peritoneum and drainage of fluid into the peritoneal cavity may occur when the epigastric route is adopted.

Pneumo-pericardium—Wenckebach (1910) observed that the introduction of air into the pericardium after the removal of the fluid prevents its reaccumulation. It is used more often now for the treatment of large pericardial effusions especially if they are tubercular (Ellman, Fenichel and Epstein, King, Levine, Patel and White). Levine recommends that the amount of air introduced should be only about half the volume of fluid removed. White has not observed good results with this method of treatment. This was done in two of our cases (Nos 7 and 9). In case 7, the introduction of air in the second instance resulted in pneumothorax on the left side with displacement of the heart to the right side, but the condition cleared within a few days. In case (9) the result was satisfactory.

SUMMARY

(1) Twelve cases of pericardial effusion are described. They are aetiologicaly classified as—Rheumatic infection 6, myxoedema 1, congenital polycystic disease of the kidney 1, unknown causation—sero-fibrinous exudation 1, haemorrhagic effusion 2 and non-inflammatory effusion 1.

(2) Symptomatology and differential diagnosis are discussed.

(3) Radiological diagnosis and electrocardiographic findings are discussed in detail.

(4) Treatment is discussed with special reference to salicylate therapy in rheumatic infection, and aspiration of the fluid with introduction of air in larger effusions.

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HYPERTENSION

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This paper is an analysis of 340 cases of hypertension admitted into the K E M Hospital from January 1932 to November 1946. Forty of these cases have been investigated by me personally and their analysis is presented separately, but no attempt has been made to draw any statistical conclusions from a series which is evidently not adequate in the number of cases studied.

Evolution of the concept of hypertension—In the middle and late 19th century hypertension was regarded solely to be a result of pre-existing renal disease.

Individual observers like Mahomed, it is true did surmise the existence of hypertension. They however, had no clear idea of the syndrome of Essential Hypertension as we recognise it today.

With the introduction of the sphygmomanometer by Riva Rocci in 1896, and its regular use in clinical medicine, the next phase of the study of hypertension was entered into. Prominent among the workers at this stage was Von Basch who coined the term "Latent Arteriosclerosis".

It remained however, for Albutt in England and Huchard in France to bring to the notice of the medical profession, a clinical entity, now well known, where high blood pressure was the predominant feature in the absence of clinically significant disease of the arteries and kidneys. They thus brought order into a jumbled group of maladies—the kidney, hypertension, arteriosclerotic disorders. Huchard even went so far as to suggest that arterial hypertension was the cause of arterio-sclerosis and to emphasize this he called it "Pre-sclerosis".

Factors regulating blood pressure and disturbances of blood pressure regulation—According to Fishberg a systolic pressure of 150 mm Hg after a period of adequate rest and on repeated examination is to be regarded as higher than normal. A diastolic pressure of 100 mm is always pathological and 95 mm is highly suspicious. This is as good a working rule as any, although numerous other arbitrary standards have been suggested.

According to current physiological teachings, the following mechanisms can conceivably produce an increase in the blood pressure.

- 1 Increase in cardiac output
- 2 Increase in blood volume
- 3 Increase in viscosity of the blood
- 4 Decrease in elasticity of the arteries
- 5 A narrowing in cross section of the peripheral vascular bed

Systolic hypertension—Clinically, states are often found where a raised systolic pressure is associated with a low diastolic reading.

A paper read at the 68th Meeting of the Seth C. S. Medical College and K. E. M. Hospital Staff Society, Bombay, held on December 14, 1946, by Dr. E. P. Bharucha, with Dr. A. Hamerid in the chair.

Examples of this are found in the bradycardia of heart block, where there is an increase in the remote output, in arteriosclerosis of the aorta and large vessels, and in the low peripheral resistance of aortic reflux and patent ductus arteriosus, where the raised systolic pressure helps to maintain the peripheral circulation. Many examples of this condition will be provided in our statistics later, they are usually compensatory in nature. This condition is also called "Divergent hypertension."

Diastolic hypertension—The diastolic pressure is dependent on the peripheral resistance which in turn hinges on the elasticity and the diameter of cross-section of the peripheral vascular bed. The peripheral vascular bed is partly under autonomic control, but not completely so, as demonstrated by the fact that completely denervated arterioles are not fully dilated being affected by substances circulating in blood. These substances affecting the peripheral bed form a formidable list and recent addition to this list is "Renin" a substance secreted by an ischaemic kidney (ischaemic due to disease or experimentally produced ischaemia as in Goldblatt's clamp experiments). Renin is activated by a pseudo-globulin fraction of the serum called renin-activator to produce a substance called angiotonin. The healthy kidney produces "renin-inhibitor" and it is possible that an imbalance between these various substances may result in a narrowing of the vascular bed and hence in a raised diastolic pressure. In health the ratio of the pulse pressure, diastolic pressure and systolic pressure is as 1 2 3, to maintain this ratio, when the diastolic pressure is raised the heart increases its output and so raises the systolic pressure. This variety of hypertension is known as "Compensated" hypertension. When the heart fails, the systolic pressure drops and we have a falling systolic with a raised diastolic pressure convergent or "decreased" or decapitated hypertension (Gallavardin).

ETIOLOGY

Incidence of hypertension—According to Fahr, in the U S A, 23 per cent of all deaths over 50 years of age are due to hypertension. Clawson gives a figure of 15 per cent. The progressive increase in the incidence of hypertension is probably associated with the longer expectation of life at the present time and the stresses and strains of modern life.

Caste and Race (Table 1, 1st Series)—Hypertension is more common amongst the occidentals than the orientals, it is almost unknown in the African Negro but is quite frequent in his brethren in the U S A living under modern conditions.

In our cases the high incidence among Christians in both the series is striking.

Age and Sex (Table 2, 1st Series)—80.9 per cent of the cases in the first series and 70 per cent of the cases in the second series were over 40 years of age as shown in table No II of the respective series. According to Clawson 90.6 per cent of his 417 cases of Essential Hypertension were over 50 years of age. Janeway states that 80 to 90 per cent were between 40 and 70, before the age of 30 essen-

tial hypertension is rare and nephritic and malignant hypertension more common. The youngest recorded case of essential hypertension is a Negro boy aged 2 reported by Tawsig and Remsen. The youngest case of hypertension in our series was a nephritic 18 years of age and the lowest age for essential hypertension was 22 years.

Sex (Table 3 of 1st series and 1 of 2nd Series)—Varying claims as to sex incidence have been made, males predominating in Janeway's series and Clawson's series and females in Boo's and Fineberg's. In the present series, the incidence of hypertension is slightly more among the males.

Heredity—The demonstration of heredity is difficult in hypertension as it occurs at a late stage, when parents and many relatives are not available for examination.

Conflicting reports present themselves in the literature. Kasanin did not find them in one of identical twins and so feels there is no heredity basis for the affection. Mass observation on the relatives of hypertensives and non-hypertensives have also lead to no conclusive results.

In our series all that could be depended on was a history of a mode of death suggestive of a hypertensive catastrophe in a relative of the patient concerned. Such a history was only definitely forthcoming in 12 cases. Even when the question was directly put to the 38 cases of this study no information of value could be obtained—only two patients could give a definite family history of hypertension (Table No. X of 2nd series).

Build (Table 4 of 1st and 8 of 2nd Series)—It is now universally accepted that the hypersthenic habitus predominates among hypertensives and this was clearly supported by our figures. 32 cases in the 2nd series of 38 had hypersthenic build.

Renal Ischaemia—As a corollary to Goldblatt's experiments an attempt was made to suggest that renal-arteriosclerosis resulting in renal ischaemia was both a cause and an effect of hypertension. In support of this is Goldring's assessment of renal blood flow by diodrast clearance, he finds that this is definitely diminished in hypertensives.

It is difficult, however, to distinguish between cause and effect in an established case of hypertension and one feels that renal ischaemia is probably an aggravating and perpetuating mechanism in most cases of essential hypertension though undoubtedly an initiator in some.

Metabolic disorders (a) *Protein Metabolism*—Newburgh, by forced feeding of rabbits and rats on a high protein diet, produced arteriosclerosis and renal lesions.

Other observers have failed to confirm his findings and feeding of hypertensives with a high protein diet have failed to raise the blood pressure. Nor is the incidence of hypertension high among Eskimos who live on very high protein diet.

Again in our series pure vegetarians constitute 27 per cent of the cases (Table 5, 1st series).

(b) *Cholesterol*—Schmidtman produced hypertension in rabbits by forced feeding with cholesterol. Again, the blood cholesterol is found to be raised in many cases of hypertension (75 per cent in many series). A raised blood cholesterol is supposed to increase the tonus of the arteriolar musculature by causing a condensation of the surface layer and sensitising to pressor substances.

Many cases of hypertension have no raised blood cholesterol.

Among the cases investigated by me the cholesterol was found to be raised in only one case (Table 23, of 2nd series).

(c) *Carbohydrate Metabolism*—Hypertensives have a diminished glucose tolerance and a tendency to hyperglycaemia.

Joslin found that hypertension occurred largely in diabetics over the age of 50.

It is probable that the same underlying constitutional defect predisposes to both conditions.

In the present series, diabetes was present in 4 per cent of cases only.

(d) *Purin Metabolism*—In cold countries, gout and hypertension are often co-existent and this as with diabetes is probably due to the underlying constitution. No information regarding this malady could be obtained in the present investigation.

Salt Retention—Ambard and Beaujard suggested that salt retention predisposed to hypertension but in the majority of hypertensives, urine and blood chlorides are normal. Unfortunately restriction of laboratory investigations prevent any observation on this aspect being made in this series.

Endocrine factors—The suprarenals, pituitary, the thyroid and the sex glands have all been suspected of being responsible agents in essential hypertension. Undoubtedly gross disturbances of these glands—Cushing's Syndrome, Simmond's Cachexia, Tumours of the Supra-renal cortex and medulla, Addison's Disease, Hyperthyroidism and Myxoedema, Ovarian Tumours and the Neoplasms—are associated with a markedly elevated or depressed blood pressure. However to pin down the responsibility in a case of essential hypertension to subclinical disturbance in function of one of these glands is more difficult, first, because quantitative assessment of various endocrine secretions in the circulation is as yet in its infancy and secondly because the endocrines form so complete an interdependent chain that it is difficult to put one's finger on the gland that was initially responsible for the mischief. For instance in many cases a hyperplastic suprarenal cortex is found associated with hypertension, this may suggest the cortical disturbance to be primary but cortical stimulation by the adrenotrophic hormone of the pituitary is difficult to rule out. It is however difficult to throw any light on this aspect of the subject from our series, and all one can say is that there were six cases of menopausal hypertension, three with metropathia and one with an ovarian cyst.

Nervous System—(a) The modern trend of attempting to find a psychological basis for all somatic disorders has not spared, and quite rightly too, hypertension. Weiss suggests that repressed rage

and anxiety result in a psychological conflict the outcome of which is hypertension

In the present series 9 cases had an emotionally labile temperament and one gave history of previous mental shock

(b) Autonomic disturbances, experimentally produced do give rise to hypertension but their role in essential hypertension is difficult to assess

Toxic Causes—(a) *Lead* predisposes to hypertension by causing an increase in arteriolar tonus in "Acute Lead Poisoning" and by producing renal lesions in the chronic stage

In the first series, 3 out of 300 cases gave a history of being lead painters or engravers, while four were mechanics who have had access to lead. In the cases studied in detail 3 cases were likely to have come in contact with lead but in none of them clinical evidences of plumbism could be found. It is regretted that laboratory evidences of plumbism could not be looked for (Table No VII 2nd series).

(b) *Tobacco* (table 6, 1st series)—Pharmacologically it has been shown by Evans and Stewart that nicotine raises the blood pressure in hyper-reactors. These effects are only transitory and many inveterate smokers have a low blood pressure

(c) *Alcohol*, (d) *Syphilis* and (e) *Focal Sepsis*—have all been incriminated as causal agents but have been shown to be only associated factor rather than cause and effect (vide table 6, 2nd series)

In our series, 27 cases of syphilis were found in 300 cases of hypertension, whereas 6 gave a history of syphilis in the recently studied cases and 4 had a positive serological evidence (Table 9 2nd series)

Allergy—Waldblatt found hypertension in members of allergic families and found that the blood pressure fell on removing the allergic factors. There is nothing to support this view. In our series out of 300 cases, 2 cases had asthma

Associated Renal Disease—(*Renal Hypertension*)—In the present series 13 cases had a previous renal affection, their distribution is shown in the table. Table 9 of the second series shows the relation of previous renal disease to hypertension in 6 cases. 4 had previous nephritis, 1 a polycystic kidney and 1 was a victim of renal calculus

CLINICAL FEATURES

Presenting symptoms—(Table 8)—Hypertension may announce its onset in a variety of ways throwing its brunt now on one system and now on another and it was this feature which rendered the elucidation of hypertension difficult prior to the introduction of the sphygmomanometer. Again, a number of cases are symptomless and discovered accidentally on examination of the fundi or blood pressure

The distribution of the presenting symptoms is given in Table 8. Of particular interest are the 63 per cent who showed nervous manifestations, the 48 per cent who showed cardiac symptoms and the 5 per cent who were asymptomatic (Table 9, 1st series)

Nervous Symptoms—(Table 11)—*Incidence*—These are present in one form or another at some time or other in the course of a hypertensive's history

One very interesting finding that has been noted in the present series is that cases with predominant nervous symptoms usually do not show any evidence of cardiovascular involvement, and the reverse of this has been found to be equally true, viz cases with early cardiovascular symptoms show, few, if any, nervous manifestations. This finding seems to concur with Fishberg's findings. There are some cases, however, where both cardiac and nervous symptoms are manifest. The incidence of the various nervous manifestations of hypertension are shown in Table 11 of the 2nd series.

Headache—This is the commonest of the nervous symptoms 46 per cent. It is probably due to cerebral arteriosclerosis and is due to an alteration in calibre of the blood vessels. It may also be due to uremia but this is unusual. Again in malignant hypertension headache is very common (10 out of 21 cases in this series) and is probably due to a raised intracranial tension associated with cerebral oedema.

Vertigo—Vertigo was the next common symptom (81 out of 190 cases, viz 41 per cent).

Mental Changes—The present theories as to the psychological basis of hypertension have been discussed in the etiological section. Here, it remains to discuss those alterations in conduct which are an effect of the hypertension. At the outset it must be remembered that our poorer classes are hopelessly illiterate and even those who are literate are not trained to be keenly aware of disturbances in mood, temper, concentration, memory etc. Further this very lack of a highly strung nervous system is in itself a protection against these symptoms becoming prominent. In short then we are dealing with a community which has neither the educational upbringing to be introspective nor the leisure to be neurasthenic (this last applies strictly to the male section). Add to this a defective history taking and one can readily explain the paucity of mental disturbances in this series as compared with foreign ones. Of those presenting nervous symptoms 12 per cent had insomnia, 4 per cent had lassitude, 15 per cent drowsiness, 05 per cent impaired concentration, 05 per cent irritability.

Minor attacks—In this group are included various angiospastic phenomena characteristic of cerebral arteriosclerosis such as transient monoplegias, hemiplegias, aphasias, fainting attacks and paraesthesias of monoplegic and hemiplegic distribution. These occurred in 14 per cent of the cases. In addition dementia may result from severe diffuse cortical involvement. It occurred in 2 of the reported cases and in 2 of the 38 cases studied in details (Table 11, 2nd series).

To be continued next month

(All the Tables of Series 1 and 2 will be printed at the end of the articles)

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Original Contributions

HYPERTENSION

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(Continued from p 152, Indian Physician, June 1947)

Major attacks (Table No 12, 1st series) —In this group are considered symptoms which differ from the above group in being more persistent and of a more severe character. These consist of hemiplegias, aphasias, convulsions and coma, all of them together or separately. Their pathogenesis consists essentially of cerebral thrombosis and haemorrhage and hypertensive encephalopathy. Without a follow up of the patient or a post mortem examination in every fatal case, it is very difficult to attach a label of diagnosis in retrospect. Certain arbitrary rules have been followed by us to arrive at some sort of diagnosis. Firstly we have followed the dictum of Walshe and Collier that all cases of cerebral haemorrhage inevitably die. Of the cerebral cases who recover, some are cases of cerebral thrombosis, others of hypertensive encephalopathy. The latter can be excluded from the former by the height of the blood pressure and the transitory nature of the symptoms in most cases. Among those who die, there are cases of all three types and without adequate post-mortem examination or a mention of repeated blood in the cerebrospinal fluid a diagnosis is impossible. This explanation is given with the deliberate idea of dispelling any complacency which may be felt as regards the authenticity of the categories into which the various cases are arbitrarily placed. Of 47 cases with major attacks 12 cases were admitted in a state of coma and 3 with convulsions. (Their origin is given in Table 12 of 1st series and Table 11 of 2nd series where 12 of the 38 cases had major attacks)

Hypertensive Encephalopathy (Table 13, 1st series) —Two elements are present here separately or together, angiospasm and elements are present here separately or together, angiospasm and cerebral oedema. The former is responsible for the transient hemiplegia, hemianopia, aphasia, etc the latter accounts for the headache, convulsions and coma accompanied by papilloedema and raised intracranial tension. In our series there were 12 such cases, and of these 3 expired two subsequently from cardiac failure and one during the attack (Table 13). It is also not unusual for hypertensive encephalopathy to occur simultaneously with a condition of true uremia as shown

in the 2nd series where both the cases of hypertensive encephalopathy had a raised blood urea (vide Table 27 of 2nd series)

Cerebral Haemorrhage—A healthy vessel will not rupture even with a high blood pressure. The presence of millary aneurysms, and areas of necrosis in the vessel wall from angiospasm or previous thrombosis have been postulated to explain the occurrence of cerebral haemorrhage. The most widely held theory today is that of Globus and Strauss who suggest that angiospasm results in softening of the brain substance, around the sclerosed vessel thus weakening the support around the vessel and predisposing it to rupture. 4 of the 38 cases in 2nd series had cerebral haemorrhage (Table 27, 1st series)

Cardiovascular System—1 *Symptoms*—(Table 14, 1st series)—Dyspnoea was the commonest cardiac symptom being present in 72 per cent of cases. Anginal attacks occurred in 33 per cent of cases in 1st series and 4 cases in 2nd series (Table No XII) and cardiac asthma in 12 per cent of 1st series. This at first seems unusual in a disease throwing its principal strain on the left heart but the probable explanation is, that the majority of cases were in combined left and right sided failure and it is well known that the supervention of right sided failure in a case of left ventricular failure results in relief of the symptoms of cardiac asthma and angina.

2 *Blood Pressure* (Tables 16 and 16-A)—In the present series the systolic pressure was usually well over 160 mm and the diastolic well over 100 mm. Average figures were between 180-200 systolic and 110 to 130 diastolic.

The highest pressure readings obtained were 280 systolic and 210 diastolic. The figures of the 2nd series are given in Table No 18.

Of the total 300 cases of 1st series in 63 per cent the pressure was fixed and 43.37 per cent it was labile. Labile cases are supposed to be early and to occur in younger people. In the 1st series the greatest systolic variations were found (240-130) in one case and (275-150) in another. The maximum diastolic fluctuations were from (170-95) and (180-90). In 32 of the 38 cases Hinc's Cold Pressor Test was performed and the results are shown in Table 19 of 2nd series. Nine of the 12 cases with a fixed pressure and 7 of the 20 cases with labile pressure gave a positive response to the test.

3 *The Arteries The Pulse* (Table 17, 1st series)—The palpatory findings of the pulse according to Moschowitz are often deceptive and functional hypertonus may be mistaken for true thickening. In the present series of the 180 cases where the pulse was noted 66 per cent had an increase in force and volume and tension, the remaining being normal.

In the new series every case had an increase in force, volume and tension.

The Vessel Wall—This was thickened in 60 per cent of the cases which were examined and in 40 per cent it was normal.

Peripheral Angiospastic Symptoms—Paresthesia, coldness of the extremities, cramps in the calves and extremities and intermittent claudication are manifestations of angiospasm supervening on an

arteriosclerotic basis In this series only 4 cases were seen with these manifestations, giving a total of 13 per cent

Rupture of Vessels (Table 18, 1st series)—Epistaxis was the commonest manifestation occurring in 50 per cent of cases with bleeding Bleeding occurred in 22 cases out of 300 (7 per cent of cases) and the sites affected are shown in table No 18 Table 27 of the second series gives the occurrence of sites of rupture in the studied 38 cases

The Heart (Table 19, 1st series)—Manifestations of left ventricular hypertrophy are frequently present in hypertension

The apex impulse is frequently not visible or palpable because of the associated emphysema so common in the sthenic type to which hypertensives belong

The frequency with which the above findings presented themselves in either series is shown in Table 19 of 1st series and Table 21, of 2nd series

The Electrocardiogram (Table 20, 1st series)—This often shows left axis deviation Master found left axis deviation in 34 per cent of hypertensives The left axis deviation in hypertensives is often accompanied by high voltage Q-R-S complexes associated with an inverted T wave in leads I and II Manifestations of myocardial degeneration may also be present

Cardiac Failure—In the present series, 33 per cent of cases suffered from both right and left sided failure and 4 per cent from left sided failure alone Arrhythmias were present in 14 cases out of 300 Thirteen had extrasystoles and one auricular fibrillation The causes of left sided failure are increased work, coronary sclerosis, supervention of abnormal rhythm and emphysema, right sided failure may be secondary to pulmonary congestion following on left ventricular failure but may occasionally be due to the thickened interventricular septum, bulging into the lumen of the right ventricle and increasing the work of the right heart This last is also responsible for those cases of hypertension which go into right sided failure without pulmonary congestion (Syndrome of Bernheim) It is also important to bear in mind that cardiac insufficiency exists even before it is clinically manifested by the classical signs An estimation of venous pressure is a very good guide and table 22 in the 2nd series of 38 investigated cases shows that of the 17 cases which showed high venous pressure only 10 had clinical evidences of cardiac failure

Coronary Thrombosis (Table 21, 1st series)—Coronary thrombosis is not uncommonly met with in hypertension With the development of coronary thrombosis myocardial insufficiency often sets in The blood pressure drops in every case but if the patient's original pressure is not known to the doctor the condition may be missed Again after the attack the pressure may remain permanently low and then the diagnosis of hypertension becomes difficult if the patient is first seen after the attack of coronary thrombosis

A fall of blood pressure in a hypertensive unassociated with car-

diac failure, rest or fever should raise the suspicion of coronary occlusion

In the present series 3 cases of coronary thrombosis were observed, their findings are shown in Table No 21

Pericarditis (Table 22, 1st series)—Three cases of uremia developed terminal pericarditis

Valvular Lesions in Hypertension—Valvular lesions occurred in five of our 300 cases Boas and Fineburg found mitral stenosis in 84 per cent of 403 cases

Renal Function in Hypertension (Tables 24, 25 and 26, 1st series)—The kidneys are affected only in 10 per cent of cases of (Benign) essential hypertension and that too usually in longstanding cases The earliest change is an impairment of water excretion later there is a defective concentration compensated for by a polyuria of low fixed specific gravity The urine may show a trace of albumen and a few hyaline casts and unless cardiac failure sets in uremia is uncommon Defective renal function has therefore to be sought for by various renal function tests

Malignant hypertension is a different proposition altogether, failure of renal function is only too obvious as shown by oliguria, symptoms of uremia, a urine loaded with red cells and granular casts, a raised non-protein nitrogenous content of the blood and changes of albuminuric retinitis in the fundi

The milder grades of renal involvement in hypertension have interested me and it is with an emphasis on this aspect of hypertension that I have proceeded with a further analysis of cases I propose subsequently to deal with this aspect in another paper The mode of assessment of renal function consists of

- 1 Routine examination of Urine—Quantity, Specific gravity, Albumin, Sediment
- 2 Water elimination and concentration tests
- 3 Non-protein nitrogenous constituents in the blood
- 4 Urea Clearance Test
- 5 Intravenous Pyelography

At this juncture I hope a slight digression on my part will be excused In spite of my most earnest endeavours it is only in a fraction of these cases that all the investigations have been performed and I feel that unless our pathology staff is increased especially on the biochemical side and X-ray plates are more freely and constantly available this investigation and others of a similar nature are doomed to frustration Under the existing conditions, the X-ray staff and our hard-pressed biochemist Mr Gokhale have rendered yeoman service and I am deeply indebted to them

Tables 24, 25 and 27 deal with the renal function in hypertension in the 300 cases of the old series and tables 24 and 25 in the new series Of all the cases of hypertension, 66 per cent showed urinary symptoms in one form or another (Table 25) Albumen, red cells and casts were present together in 29.14 per cent and non-protein nitrogen values of over 50 mgm 100 cc were found in 24 per cent of cases of the 1st series and 6 cases of the recent series

In 4 cases of that series the urea clearance was also impaired These were cases of gross renal involvement

Mild grades of renal impairment has been looked for in the 38 cases examined later and the result is shown in Table 25 of that series Of the 32 cases so investigated 13 had impaired renal function as shown by inability to concentrate the urine adequately

Eye in Hypertension (Table 25)—Changes in the fundi are very frequent in hypertension and are of diagnostic and prognostic significance In the 1st series, evidence of fundal arteriosclerosis was present in 98 of 187 cases in which the fundi were examined, i.e. in 71 per cent of cases This corresponds to figures given by Fishberg, O'Hare and Walker Of the 31 cases out of 38 cases of the recent series where the eye-grounds were examined 22 cases had evidence of benign arteriosclerosis and 7 showed haemorrhages, 5 had exudations and only 1 had papilloedema (Table 26)

Examination of the fundi is useful diagnostically from two points of view Firstly it catches the early cases as a spasm of the retinal arterioles is said to precede any sustained rise of blood pressure Secondly retinal arteriosclerosis persisting as it does even after the blood pressure falls may help in the diagnosis of antecedent hypertension

The distribution of the fundoscopic abnormalities is shown in Tables 26 and 27 of the 1st and No 26 of the 2nd series Hypertensive neuro-retinopathy which is diagnostic of malignant hypertension was present in 25 cases (18.2 per cent) 24 of these were due to malignant hypertension and one to chronic nephritis

Malignant Hypertension (Table 28)—Considered at first by Volhard and Fahr to be a combination of acute nephritis and hypertension, it was later shown by Keith Wagner et al to be the result of sustained and very high diastolic tension resulting in arteriolar necrosis and cerebral oedema

The characteristic features of malignant hypertension are its early age, high diastolic pressure, severe fundal changes with papilloedema, early renal involvement and a rapidly fatal course

These facts are clearly brought out in our 24 cases

TABLE 28

Age incidence	22 cases	below 55
Diastolic pressure	19 cases	over 130 mm
Papilloedema	21 cases	
Impaired renal function	14 cases	out of 24
Mortality	9 cases	out of 24

Alimentary and Respiratory Symptoms (Table 30A-30B)—Individually symptoms referable to the Alimentary and Respiratory Systems are shown in Tables 30A, and 30B In the new series the incidence of these symptoms is shown in table 14

Complications (Table 31)—As in the symptomatology, so in the complications the cardiovascular and nervous manifestations hold paramount place In the present series, 50 patients expired out of a total of 300 cases and in them cardiac failure, in one form or another occurred in 12.6 per cent and was responsible for 52 per cent of deaths Cerebral complications accounted for 16 per cent of deaths and renal ones for 16 per cent of deaths

the 2nd series shows the incidence of various complications and 21 of the 38 cases had one or the other of cardiovascular symptoms and of these cardiac failure was of most frequent occurrence. Next in importance come the cerebral complications like thrombosis, haemorrhage, minor attacks or hypertensive encephalopathy.

PROGNOSIS OF HYPERTENSION

I *Duration of Hypertension*—No satisfactory conclusion can be arrived at in our series of cases due to lack of follow up.

II *Sex* (Table 33)—The mortality in females in our series was definitely lower—3 per cent (males 20 per cent) which corresponds to Paulein's figures of 3.8 per cent mortality in females (males 54.1 per cent).

III *Age* (Table 32)—The mortality is higher when hypertension develops early in life, because these cases tend to become malignant.

IV Prognostic Significance of Blood Pressure (Table 34)—

1 The higher the systolic tension the worse the prognosis. There is an increase in mortality from 14 per cent to 18 per cent with increasing systolic pressure groups.

2 The height of the diastolic tension is an even greater aid to prognosis and whereas the mortality with diastolic pressures of 80 to 120 mm is 13.4 per cent, for pressures between 150 to 210 mm is 34.5 per cent.

3 The mortality is also higher in the fixed blood pressure group (74 per cent), than the labile ones (26 per cent).

V *Prognosis with Myocardial insufficiency*—Of the 134 cases admitted with cardiac failure 33.15 per cent expired as a result of cardiac failure. With first attacks of cardiac failure the prognosis is good but with subsequent attacks it progressively deteriorates.

VI *Anginal attacks and cardiac asthma*—Although 23 and 18 cases respectively of anginal attacks and cardiac asthma were admitted in this series, only two died in each group indicating that it is the remote prognosis which they affect rather than the immediate one.

VII *Fundi in hypertension* (Table 35-B)—Patients with hypertensive neuro-retinopathy usually succumb within a year from the diagnosis.

As regards retinal arteriosclerosis, it carries with it two implications, firstly that the hypertension is a long-standing affair and secondly that there it probably affects the remote prognosis.

VIII *Renal Failure* (Table 35)—In a young person with a defective concentration test the course is likely to be rapidly fatal within a year.

In an elderly person the finding is not of such significance and the disease progresses very slowly.

The present series showed that 33 per cent of cases admitted to the hospital with impaired renal function expired in the hospital.

IX *Cerebral symptoms in prognosis*—Of the 190 cases in this series with cerebral symptoms 28 per cent expired. Cerebral symptoms in general are of ill omen and presage a cerebral catastrophe among them.

X Complications in prognosis (Table 36) —The percentage mortality of the various complications is given in Table No 36. Cardiac, renal and cardio-renal failure seem the most deadly once they set in.

CONCLUSIONS

The study points out certain facts which require particular notice.

Aetiology —The incidence is particularly high amongst the Christians, the males predominate slightly over females and the incidence of essential hypertension is not common under the age of 40. The youngest recorded case is 21 years old.

Symptoms —The nervous symptoms predominate over others being found in as many as 63 per cent of all cases. Cardiovascular symptoms are next in frequency. It is not common to find both the systems being affected at the same time. Mental symptoms are not very frequent in our series and it is difficult to inquire about the symptoms in the hospital class of patient. 5 per cent of cases are symptomless. It is particularly important to note that raised venous pressure precedes definite clinical evidences of congestive cardiac failure and it is desirable that venous pressure should be estimated in every case so that treatment can be instituted early. Another important point is the estimation of renal function by a simple procedure like concentration and dilution and specific gravity tests. It would be very useful in guiding the treatment and in judging the prognosis to find out the earliest evidence of impaired renal efficiency. The visualization of the eye-grounds is another simple procedure which yields information of much value with regards to diagnosis and prognosis of the case. Once evidence of inalignant hypertension appears the prognosis is quite different from that of benign hypertension.

Prognosis —What materially alters the prognosis of hypertension is the onset of the malignant phase. This is almost invariably fatal in a short while whereas a case of benign hypertension may go on with care for as many as 20 years.

Again a case of hypertension at a relatively younger age is more likely than not going to be malignant in type and hence carries a graver prognosis. Males, it is found, are an easier prey to the disease than females. The onset of any complication naturally cuts short the span of life and of these cerebral haemorrhage is the worst offender. Once either cardiac failure or uraemia sets in it gives cause for anxiety and the latter though not so frequent as the former is naturally of a very grave significance.

In conclusion it would not be out of place to expect that in future we might be able to investigate cases of hypertension in a better way with particular reference to laboratory and radiological investigations of the kidneys and to treat them with greater success by catching them early. In our quest for a more successful outcome of the results of our treatment it is not too much to expect an active co-operation from the pharmacologists and from the surgeons.

In conclusion I wish to thank the Dean, my hononaries Dr Hameed and Dr Yakil for their constant encouragement and the complete freedom of action allowed me with regard to admission and investigation of cases. I am also very thankful to our housemen and registrars and those of other units, to our biochemist Mr Gokhale and to the x ray staff for their unstinting co operation.

DISCUSSION

Dr N D Patel remarking on the high incidence of hypertension in Christians, wondered whether their mode of life was responsible for it, because racially they were not different from other Indians. As regards the low incidence of hypertension and coronary disease in women, he ascribed it probably to the effects of female hormones. He suggested to the speaker the separation of Essential Hypertension from cases of chronic nephritis. He also enquired as to the incidence of hypertension resulting from malarial nephritis. He drew attention to Table 21 and was critical of the high percentage of the normal size of the heart. Dr Patel deplored the inadequacy of clinical notes in hospital records, and was critical of conclusions drawn from such inadequate heterogeneous sources.

Dr R G Dhayagude remarked that no mention had been made to Paroxysmal Hypertension. In this connection he cited an autopsy reported previously to this Society where a Pheochromocytoma was detected in the medulla of the suprarenal.

Dr K A J Lalkaka was of the opinion that persons suffering from a repression anxiety neurosis found a fair number of subjects of this disease. He emphasized psychological treatment in the alleviation of symptoms in cases where a secondary neurosis developed.

Dr S G Joshi cited a case of Paroxysmal Hypertension where there was fluctuation hour to hour and day to day, persisting for three months prior to his retirement from active service. When observed three years later the blood pressure was normal. Epistaxis occurring in Hypertension, he added, was known to be a safety valve and enquired as to how long a patient was to be allowed to bleed.

Dr A. V. Baliga reported a case of young college student which was diagnosed as malignant hypertension with loss of vision in one eye and impairment in the other. There was a history of renal colic on the left side. On investigation a non-functioning atrophic kidney was detected on the left side. Nephrectomy was followed by blood pressure becoming normal on the fourth day and has remained at this level to date (two years). He also recovered his vision completely.

Dr R. G. Ginde reported a case similar to that of Dr Baliga. He enquired of the speaker whether any of the patients were subjected to surgical treatment. He also inquired if any of these cases of essential hypertension were treated with Potassium Thiocyanate.

Dr A Hameed congratulated the speaker and advised that further work be done on the subject.

Replying to Dr N D Patel, Dr E P Bharucha agreed to the necessity of separating essential hypertension from those following nephritis. He did not come across any cases of malarial nephritis causing hypertension. In reply to Dr Joshi he remarked that he was unable to advise as to the time, hypertensives with epistaxis should be allowed to bleed. In reply to Dr Ginde, the speaker said he had no experience of Potassium thiocyanate in the treatment of hypertension.

TABLES
FIRST SERIES

TABLE 1 Incidence of Hypertension

Caste	Hypertension Total Percent		Total Admission	% of Total Admission
Hindus	140	46.8	117,743	68
Muslims	45	15	26,837	15.70
Christians	100	33.3	23,921	18.00
Others	15	5.0	4,230	2.41

TABLE 2 Sex Incidence of Hypertension in various age groups

Age	Male	%	Female	%	Total cases	Total percent
10—20	1	33	2	67	3	1.0
20—30	8	80	2	20	10	3.3
30—40	35	70.2	8	24.0	43	14.4
40—50	73	78.5	20	21.5	93	31.0
50—60	91	79.2	10	20.8	77	25.6
60—70	30	67.2	10	32.8	58	19.3
70—80	10	62.5	0	37.5	10	5.4

TABLE 3 Sex Incidence of Hypertension

Cases	Total No Hyp cases	Percentage of Hyp cases	Total Admissions to Hospital 1932—1945	Percentage of admissions
Males	227	75.0	123,330	71.0
Females	73	24.4	47,760	28.1

TABLE 4 Build in Hypertension

Build	Total	Percent
Hypersthenic	106	72.0
Sthenic	69	22.0
Asthenic	14	5.2

TABLE 5 Diet

Diet	No	Percent
Mixed	207	72.0
Vegetarian	68	27.0

TABLE 6 Incidence of Tobacco & Alcohol among hypertensives

Addiction	Total	%
Tobacco alone	57	22
Alcohol alone	21	8
Tobacco & alcohol	71	30
Nil	106	40

TABLE 7 Renal causes of Hypertension

Nephritis	9
Pyelitis	2
Renal Calculi	2

TABLE 8 Symptom groups in Hypertension

Symptoms	Total	%
Nervous	190	68
Cardiac	146	48
Alimentary	47	16
Respiratory	43	14
Renal	27	9
Peripheral	1	0.3
Rupture	14	4.7

TABLE 9 Symptomless Cases of Hypertension.

Cellulitis of the face	1
Dysentery	1
Syphilitic paraplegia	1
Metropathia	1
Found on routine exam	1
Accidentally found	7
Diabetes	1
Asthma	1

TABLE 10 Cases with one symptom only

Symptoms	Total out of 300	Percentage of cases
Nervous	92	30.66
Cardiac	28	9.33
Epistaxis	9	3

TABLE 11 Nervous symptoms as percentage of Total Nervous Symptoms

Symptoms	% of Nervous	% of Total
1 Impaired Concentration	0.5	0.3
2 Irritability	0.5	0.3
3 Impaired Memory	1.0	0.7
4 Insomnia	12.0	7.7
5 Lassitude	4.0	2.7
6 Drowsiness	1.5	1.0
7 Headache	48.0	30.7
8 Blood vision	12.0	7.7
9 Throbbing head	2.0	1.3
10 Minor attacks	14.0	8.7
11 Convulsions Coma with hemiplegia	23.5	17.7
12 Giddiness	41.0	26.0
13 Weakness	7.0	4.7
14 Tinnitus	1.7	1.0
15 Pain in extremities	0.5	0.3

TABLE No 12 Major Attacks

Cerebral Thrombosis	20
Cerebral Haemorrhage	6
Encephalopathy	10
Cerebral complications with Cardiac failure	11
Encephalopathy with renal failure	1

TABLE No 13 Analysis of cases of Encephalopathy

No	4	3	5
Age	45-62	42-55	15-44
Origin—E. H.	4	3	4
—Neph			1
Blood Pressure			
—Systolic	230/230	220/210	160/190
—Diastolic	200-130	130	85-140
Renal Function —			
—Impaired			
—Normal	2	2	4
—Not mentioned	2	1	1
Fundi —			
—Normal		2	4
—Not mentioned		1	1
—Retinal Scl.	3		
Results:—			
—Relieved	3	2	4
—Expired	1	1	1
	Cardiac Failure	Cardiac Failure	

TABLE 14 Cardiac Symptoms

Symptoms	Percentage Total	Percentage Heart Symptoms
Dyspnoea	35.83	75.8
At rest	18.8	27.89
On Exertion	19.7	44.1
Orthopnoea	3.8	8.81
Palpitations	10.68	22
Precordial pain	5.88	11
Anginal attacks	7.66	15.9
Oedema	21	48
Ascites	0.88	1

TABLES 15, 16, 16A

Systolic pressure (Benign)			Systolic Pressure (Malignant)		
Systolic	No of cases	%	Systolic	No of cases	%
125—180	72	24	125—180	0	0
180—220	138	46	180—220	8	28
220—280	90	30	220—280	16	67

Diastolic pressure (Benign)			Diastolic Pressure (Malignant)		
Diastolic	No of cases	%	Diastolic	No of cases	%
65—120	140	49.7	65—120	5	20.88
120—150	128	42.0	120—150	8	33.8
150—210	28	7.7	150—210	11	43.84

TABLE 17 The Vessels

Pulse	Total No	%	Vessels	Total No	%
Increased force volume, tension	80	66.7	Arteriosclerotic	45	60
Normal	40	33.8	Normal	80	40
Not mentioned	180		Not mentioned	225	

TABLE 18 Bleeding

Epistaxis	11	52.4
Haemoptysis	8	14.8
Haematemesis	7	4.4
Cong. Haemorrhage	2	0.5
Haematuria	2	0.5
Menorrhagia	1	4.8
Piles	1	4.8

TABLE 19 The Heart

Heart	Total	%
Apex normal	71	24
Heaving	68	21
Impalpable	185	55
Size Normal	186	62
+	54	18
++	33	11
+++	4	1.8
Not found	11	3.6
Thrill	1	0.8
1st sound booming	47	15.6
2nd Sound accentuated	148	44.88
Brut	52	17.88

TABLE 20 E C G

	Total No	%
Left axis deviation	30	50.6
S T deviation	5	9.48
Flat T	6	11.32
Inverted T in 3 Leads	10	18.86
Q R-S slurring	2	8.77
Normal	10	18.86
Not taken	247	

TABLE 21 Coronary Thrombosis

Age Sex	Pressure	Complications	Results
1 M 63	210/120	Right sided failure	Expired in 8 days
F 50	230/130	Nil	Recovery 84 days
F 60	150/110 to 130/110	Nil	Recovery 9 days

TABLE 22 Pericarditis

Age	Etiology	Renal Function	Complications	Result
1 M 40	Nephritis	Impaired	Cardiac Failure and Uremia	Expired 8 days
M 35	Nephritis	Impaired	Cardiac Failure and Uremia	Expired 7 days
M 42	Malignant Hypertension	Impaired	Cardiac Failure and Uremia	Expired 7 days

TABLE 23 Vascular Lesions

Murmur	No	B P	K T
Diastolic at base	1 Aortic regurgitation	250/100	Negative
	1	177/70	Negative
Systolic & Diastolic			
(a) at base	1 "	250/125	Negative
(b)	1	180/90	Not done
(c) at apex	1 Mitral		

TABLE 24 Urinary Symptoms

Symptoms	Total cases	% Total	% Urinary
Oliguria	6	2	22.2
Nicturia	0	2	22.2
Poluria	8	2.66	29.0
Uremia	2	0.66	7.4

TABLE 25 Urine.

Urine	Total cases	%
Normal	100	40.5
Albumen	75	30.36
R B Cs Casts albumin	72	29.14
Not mentioned	53	

TABLE 26 Non-protein Nitrogen

N P N	No. of cases	%
Normal	52	52
32.5—50 mgms	24	24
50—100	18	18
Over 100	0	0

TABLE 27

Fundi	No. of cases	%
Normal	39	39.5
Arterial spasm	0	4.3
Retinal sclerosis	45	32.3
Haemorrhage & exudates	22	16
Papilloedema	25	18.2

TABLE 28 Cases of Malignant Hypertension

No. of Cases	10			0	
	200/180 200/100	100/130 230/150	180/00 245/120	5 cases	
Blood Pressure	2	7	1	3	cases
Age	20-30 30-55 55-70	7	4	10	"
Renal Function	N Imp Not done	3 7 1	2	3	"
Fundi	Normal Benign Malignant	1 0	1 0 7	1	"
Complications & Result	Expired	3 Cardio failure	3 cardiac failure and uremia	3 card & Ure	mia
	Relieved	4 Card failure	5 cardiac failure	2 with card and cerebral	
	Otherwise	1 cardiac with urem 1 card Fail	1 Cerebral haemorrhage		

TABLE 29 Results

Total	Percent.
50	10
201	87
49	16.3

TABLE 30 Stay in Hospital

Minimum	Maximum
1	195

TABLE 30A Percentage frequency of individual symptoms pertaining to the alimentary system.

Symptoms	Total No	Percent
Anorexia	21	44.7
Constipation	13	27.8
Flatulence	12	25.5
Vomiting	16	34
Abdominal pain	24	51
Hiccough	1	2

TABLE 30B Relative incidence of various respiratory symptoms

Symptoms	Total No	Percentage
Dyspnoea	18	32.1
Cough	34	60.7
Haemoptysis	2	3.5

TABLE 31 Complications in expired cases

Complications	Total No	Percentage
Right sided failure	75	25
Left sided failure	12	4
Both sided failure	9	3
Cerebral	26	8.7
Encephalopathy	9	3
Uraemia	2	0.7
Cardio cerebral	11	3.7
Cardiac with uraemia	6	2
Cerebral & uraemia	2	0.7
Nil	148	49

TABLE 32 Percentage mortality of different Age groups

Aged	Admitted	Expired	Percentage Mortality
10 — 20	3	1	33
20 — 30	10	2	20
30 — 40	43	0	21
40 — 50	03	10	17 2
50 — 60	77	10	13
60 — 70	58	8	13 8
70 — 80	60	7	18 75

TABLE 33 Prognosis with sex.

Admitted males	Expired males	Percent mortality males	Percent mortality females	Expired females	Admitted females
227	44	20	3 4	6	173

TABLE 34 Prognosis & Blood Pressure

Systolic B P	Total admissions	Expired	Percent
125 — 180	72	10	14
180 — 220	138	23	16 6
220 — 280	00	17	18 8
Diastolic			
65 — 120	140	20	13 4
120 — 160	128	22	17 1
160 — 210	23	8	34 5

TABLE 35 Prognosis in relation to symptoms

Symptoms	Total admissions	In Expired	Percent.
Angina	23	2	9 0
Cardiac	140	38	33 5
Cardiac asthma	18	2	11 1
Cerebral	107	34	27 0

	Ben	Mal	Ben	Mal	Ben	Mal
Fundi	73	25	14	0	19 18	70
Impaired renal	48			18		37 25

TABLE 36

Prognosis with Complications Complications expressed as % Mortality

	Total	Expired	% Mortality
Right sided failure	75	10	21 4
Cerebral accidents	26	6	23
Left sided failure	12	4	33 3
Cardiac failure and cerebral complications	11	7	63 63
Combined failure	9	6	66 6
Encephalopathy	9	1	11 11
Cardiac with Uraemia	6	5	83 33
Cerebral complications with Uraemia	4	1	25
Uraemia	2	2	100
Nil	148	2	1 3

SECOND SERIES

TABLE 1 (Sex)

TABLE 2 (Age)

M	27	20	20-30	31-40	41-50	51-60	61-70	71
F	11	2	2	6	10	11	7	Nil

TABLE 3 (Caste)

TABLE 4 (M/W/S)

TABLE 5 (Diet)

H	M	CH	P	Married	33	Vegetarian	12
10	4	12	3	Single	4	Mixed	10
				Widow	1		

TABLE 6 (Addictions)

TABLE 7 (Occupation)

None	13	Manual	8	Pressman	1*
Alcohol	Nil	Priest	3	Cook	2
Tobacco only	4	Typist	2*	Sailor	1
„ with Alcohol	21	Sadhu	2	Telegraphist	1
		Tailor	1	Teacher	1
		II Wife	11	Student	1
		Peon	1	Nil	3
				*contact with lead	

TABLE 8 (Build)

TABLE 9 (Previous Illness)

TABLE 10 (Family History)

Asthenic	3	Haematuria	2	Positive	2
Sthenic	2	Nephritis	4 *	Negative	30
Hypersthenic	32	Syphilis	0 - (+K4)		
		Diabetes	1		
		Renal Calculi	1*		
		Polycystic Kidney	1*		

TABLE 11 (Nervous Symptoms)

/	Mental fatigue	8	Throbbing in head	2
	Irritability	21	Minor attacks	2
	Impaired memory	8	Giddiness	5
	Insomnia	13	Tinnitus	
	Lassitude	18	Parasthesia	
	Drowsiness	8	Weakness	1
	Headache	22	Major attacks	12
	Blurring of vision	17		

TABLE 12 (Cardiac symptoms)

TABLE 14 (Respiratory symptoms)

Dyspnoea				
	<i>Slight exertion</i>	25		
	<i>Rest (c c f)</i>	10		
Palpitation		12	Cough	10
Precordial distress		10	Proxymal	
Attacks of angina		4	Breathlessness	0
Oedema of feet			Haemoptysis	Nil
Ascitis				

TABLE 15 (Alimentary symptoms)

TABLE 16 (Renal symptoms)

Anorexia	3	Oliguria	7
Flatulence		Nocturia	5
Vomiting	1	Polyuria	4
Pain in abdomen		Oedema	3
Heartburn			
Constipation			

TABLE 17 (Rupture symptoms)

Haemoptysis	2
Epistaxis	4
Haemetemesis	2
Conjunctival haemorrhage	2
Retinal haemorrhage	2
Haematuria	2
Menorrhagia	1
Bleeding piles	2

TABLE 18 (Blood Pressure)

Systolic	150-200	24
	200-250	13
Diastolic	250	
	95-120	21
	120	17
	17	
Labile	21	

TABLE 19 (Hine's Test)

Cases tested	32
Fixed pressure	12
Labile pressure	20
Cases of fixed pr. which gave a response to test	0
Cases of labile pr. which showed a marked alteration in pressure on test	7

TABLE 20 (Vessels) Thickened and Tortuous

Radial	20
Brachial	21
Temporal	21
Normal	10

TABLE 21 (Heart).

Apex beat	Not felt	11	Systolic bruit	0
	Normal	10	Gallop Rhythm	
	Heaving	17	Pulsus Alternans	
Size	Enlarged	16	Raised Ven Pr	17
	Normal	22	C C F	10
Accentuated 2nd aortic		25/22		
1st Mitral				

TABLE 22. (Venous pr & C C F)

Cases Investigated	32
Ven pr + without signs of evident failure	7
Normal V Pr	15
V P + with C C F	10

TABLE 23 (Serum cholestrol)

No investigated	10
Normal	15
Raised	1

TABLE 24 (Urine Exam)

Sp Gr	Below 1002	Nil
Examined in 32 cases	1002-1010	12
	Above 1010	20
Albumin		8
Sugar		Nil
R B C		0
Casts		0
R B C. & Casts		0

TABLE 25 (Renal Func.)

Conc & Dilution	No Invest.	32
	Normal	10
	Imp Conc	13
	Imp Dilu	0
	Imp Conc & Dilu	0
Urea Clear	No Invest.	10
	Normal	15
	Impaired	4
N P N	No Invest	21
	Normal	15
	Raised	6

TABLE 26 (Fundus Exam)

No Invest	31	} Benign
No of veins	22	
Spasm of Art	22	
Sliver wiring	22	
Linking	7	
Haemorrhage	7	} Malignant
Exudate	5	
Papilloedema	1	

TABLE 27 (Complications)

Left sided failure	5	} *
Right sided failure	10	
Angina	2	
Coronary thrombosis	2	
Pericarditis	Nil	} *
Abnormal Rhythm	Nil	
Asthma	2 *	
Acute Pulmonary Oedema	2	
Cerebral Thrombosis	3	} †
Cerebral Haemorrhage	4	
Minor Attacks	1	
Hypertensive Encephalopathy	2	
Uræmia	2	
Peripheral gangrene	Nil	
Intercurrent infection	Nil	

* Cardiovascular † Nervous

Clinical Case Record

CHOLEDOCHUS CYST OR CONGENITAL CYSTIC DILATATION OF THE COMMON BILE DUCT —N D PATEL, M.D

X Y female, aged 18, felt sharp colicky pain in the upper abdomen on April 19, 1947. During the night she vomitted several times and had several bouts of severe abdominal pain which doubled her up. The next day there was no pain but the temperature rose upto 102°F with shivering. During the night the temperature subsided but the colicky pains returned. Intermittant temperature and severe abdominal pains persisted till April 23, when I saw her with Dr N A Sukhtankar. During this period there was no disturbance of bowels or micturition.

The physical examination on the fifth day of illness (23-4-1947) showed a well-nourished young woman, in recumbent position, with legs slightly flexed, though she could extend them without any discomfort if asked to, and preferring to lie on the left side rather than on the right. The temperature, pulse, respiration and colour of the skin and mucous membrane were normal. Except for the bouts of pain, which she complained were unbearable and made her bawl out in agony, she was very cheerful and did not look ill, so much so that one was inclined to consider her bouts of pain 'psychic or hysterical'. The abdominal examination revealed normal skin, movements, and muscles except for slight tension in the right upper quadrant. On deep palpation one could feel a definite lump in the epigastrium more to the right than to the left. The mass was about 3" x 3" in size, soft in feel, painful on deep pressure and dull to percussion. The liver, gall-bladder or spleen were not palpable. The patient complained of pain in the back at the lower end of scapula and in the middorsal vertebrae. She resented examination of the abdomen saying that this brought on her sharp colicky pains. There were no physical signs of any disease in the lungs, heart or nervous system.

The stools and urine were normal, and a blood slide taken a day before showed polymorphs 87 per cent, lymphos 17 per cent, and absence of malarial parasites

The past history was essentially negative, except that she used to suffer from colicky pain, headache and sometimes vomiting on hot summer days. Father and mother were alive and well, of the six children they had the patient was the only surviving child, the other five having died in infancy or childhood. Details of their illnesses were not available.

A provisional diagnosis of some biliary disorder was made and belladonna, coal-tar analgesics with luminal, a saline mixture, sulphadiazine, urotropine, and quinine which were being given from the beginning of the illness were continued. She had a comparatively comfortable day, free from pain, but during the night about 2 a.m. the severe pains started, and she complained of such agony that it was considered necessary to inject morphia with atropine, which allowed her to get some sleep. The next day (6th day of illness) there was no pain but the temperature rose to 104°F and the abdominal pains started early in the morning were extremely severe when I saw her about noon. She was writhing in pain bawling out extremely loudly with each paroxysm, which showed the usual reactions associated with severe pain—perspiration, goose flesh skin, upstanding hair and collapse which made her dazed and semi-conscious for a time. The physical examination now showed a definite tinge of jaundice, and the mass in the upper abdomen was larger and visible. She resented the examination of the mass and of the gall-bladder area. Now the urine showed the presence of bile and the blood examination a total count of 9400 white blood cells with 87 per cent polymorphs. A consulting surgeon was called in to see the patient in the evening, who suggested that the patient was suffering from cholecystitis with perhaps gallstones but surgical intervention at this stage was not called for, and advised to continue the treatment with sulphadiazine, penicillin and glucose.

This treatment with palliatives was continued for the next four days, but it made no difference to the paroxysms of pain or to the intermittent fever. The tumour during this period of observation showed some variation in size from day to day, the jaundice deepened and the patient definitely looked bad and ill. During the night of April 29 (11th day of disease) the temperature shot up to 107.8°F. Ice packs and ice water enema controlled the hyperpyrexia, but the dazed and collapsed state continued till the morning. The patient was transferred to a nursing home under a surgeon (Dr K. G. Munsiff), for exploratory operation. Before the operation, penicillin, streptomycin and quinine injections were given for three days, without any benefit. The total white blood count rose to 19,500 per cmm with 91 p.c. polymorphs, the van den Bergh was direct immediate positive, icteric index was 52. During the night of May 2, (14th day of disease) she again developed hyperpyrexia, the temperature rising upto 108.2°F with marked collapse. On opening the abdomen, on the afternoon of May 3, (15th day of illness), the gall-bladder was found to be congest-

ed and tense, smaller in size than normal if anything, and stood up like an upturned thumb. It was quite free from any adhesions. The liver was normal in consistency and free from any congestion. There was a mass in the right upper quadrant lifting up the liver above, and displacing the stomach and distorting the duodenum. Careful palpation of the biliary system revealed no stones in the gall-bladder or in the ducts. The palpation of the mass did not show any definite outline, it was tense in feel, free from any pulsation, and suggested a collection of pus or bile. A needle was inserted in it and 16 oz of thick bile was withdrawn. The cavity was washed out with ether and a considerable amount of inspissated bile came out, but no stone. The examination of this bile showed presence of red blood cells, pus cells, and gram negative bacilli but no crystals or stones. During the night the patient had another bout of hyperpyrexia with collapse which terminated fatally next morning, on the 16th day of illness. On further examination of the aspirated bile, the gram negative bacilli were reported to be Eberthi typhi, satisfying all the cultural and serological tests.

Congenital cystic dilatation or a diverticular pouch of the common bile duct is a rare malformation, only about 120 cases being on record. Over 80 per cent of these reported cases were in females, the majority of whom were under fifteen years of age. In all the reported cases there was a large, tense, spherical, cystic tumour of the upper right quadrant of the abdomen just below the liver, displacing the stomach and duodenum, and it contained normal or infected bile, but never any stone. Pain occurred in all cases, which was paroxysmal and varying in intensity. Choledochus cyst produced partial or complete obstruction of the common bile duct and jaundice occurred in most of the cases depending on the degree of obstruction, which also determined the amount of bile in the urine and stools. Fever was only present when the contents of the cyst were infected. The diagnosis of this rare condition is suggested by a history of colicky pain in a young girl, with a tumour in the upper right quadrant of the abdomen, who develops jaundice or fever, and who is quite healthy and happy when not in pain. The treatment is only surgical, though it carries a very high mortality, no case of spontaneous recovery is reported.

In the case reported here the high fever with a tendency to hyperpyrexia, and the presence of *B typhosus* in the bile are interesting findings. There was no clinical evidence of typhoid fever. Was she a typhoid carrier or did she get typhoid infection, where typhoid bacilli, finding a favourable culture medium in the diverticular pouch full of bile, grew luxuriously and produced severe toxæmia and repeated bouts of hyperpyrexia? It is interesting to note that Sulphadiazine and Penicillin in heavy doses for 8 days and Streptomycin 2 Gm per day in 3 hourly injections for 3 days had no effect on the course of the infection.

Critical Notes and Abstracts

FUNGUS INFECTIONS OF THE SKIN D T PREHN (*Urol & Cut Rev* 1946 50 416-418) A formula containing salicylic and menthol and camphor has been found to act almost specifically against fungus infections of the skin. Although described before, the method of preparation and the manner of treatment apparently are not clearly understood. It is the object of this article to more lucidly describe its preparation along with further recommended uses.

The fundamental formula is made of salicylic acid (5 Gm), menthol 5 (Gm) and camphor (10 Gm) with a vehicle (80 Gm). These 3 crystalline chemicals when triturated together eutectically dissolve into solution. Making them into a solution is the proper first step in the preparation of the prescription. The vehicle for this liquid formula can be either a powder, a solution or an ointment. For the routine treatment of mycotic infections of the glabrous skin, the powder vehicle is preferred. Finely powdered boric acid (40 Gm) is thoroughly mixed with talcum (40 Gm), starch, kaolin, fullers' earth, aluminum silicate, chalk or other powders can be used instead of talcum. This boric acid talcum mixture is then vigorously triturated into the formula solution of camphor, menthol and salicylic acid. A fine sticky powder should be the end result. To make sure the final product is a gritless, smooth powder it should be rubbed through a fine mesh colander. This will remove any granular property. This is necessary as the powder is applied to the diseased and surrounding skin by inunction. It seems necessary to emphasize here that the prescription cannot be made up as a dusting powder. The powder is adhesive, pasty and soft-almost ointment-like in character. It cannot be dusted on the skin but must be vigorously rubbed into the skin.

The powder cannot function through thick callosities, sodden masses, crusts or thick roofed blisters. They must be removed before improvement can be expected. After these obstructions are removed or as many as are possible at the time of treatment, the skin is thoroughly dried before vigorously rubbing the powder into the diseased and surrounding skin. The treatment may be in the morning, daily or oftener as the case may be, entirely depending upon the progress of the disease. As the condition improves the intervals between the treatments can be increased until the skin is entirely new and clear, having the normal healthy appearance without evidence of disease.

The powder is prescribed in 100-Gm lots. It is put up on a waxed or cellophane paper 18 inches square. Then the paper is opened and spread out with the powder-pile in the center, the foot is put on the paper and the powder is vigorously rubbed into the diseased and surrounding skin, leaving some packed in between the toes if they are infected, some in the socks and also some in the shoes, as walking.

about will continue the inunction of the powder into the foot. Thus, when the treatment is finished, what is left of the powder can be wrapped up in the waxed paper, leaving no mess on the floor, saving all the powder that was not used and the powder can be conveniently stored away for the next treatment.

Eighty-six cases of pruritus ani have also been treated successfully. For patients who complain of smarting on the first applications the powder can be diluted with talcum. This is occasionally necessary on other acute conditions elsewhere especially around the scrotum. The simple application of common sense will direct the proper procedure.

The success of this formula in clearing up fungus skin infection has added a new use for it. If the skin infection does not clear up under proper treatment with this powder it is apparently not a fungus infection.

PENICILLIN INHALATION IN PULMONARY DISEASE J. H. HUMPHREY and H. JOULES (*Lancet*, 1946 17 221-226). Eighty patients with various types of pulmonary infection have been treated by inhalations of penicillin. Forty-six showed much improvement and 17 others were classed as "improved." The type of disease involved and the results of therapy are listed in Table I.

TABLE I
CLINICAL RESPONSE IN 80 CASES TREATED BY PENICILLIN INHALATIONS

Condition	No of cases	Much Improved	Improved	Not Improved
Chronic bronchitis	20	15	5	0
Bronchiectasis	18	12	4	2
Respiratory infection with congestive heart failure	15	7	4	4
Pneumonia and generalised bronchitis	11	7	4	0
Lung abscess	5	3	0	2
Suppurative pneumonitis	4	0	0	4
Silicosis + bronchitis	3	2	0	1
Atypical pneumonia	4	0	0	4
Total	80	46	17	17

Our criteria of "much improved" were subsidence of all acute changes and signs of toxemia, together with very marked or complete reduction of cough and of the amount of sputum, while those for "improved" were subsidence of acute changes and signs to toxemia, with definite diminution of cough. The sputum in these cases was rendered much more mucoid and less purulent, but was only moderately diminished in amount. Pyrexia in acute bronchitis and bronchiectasis with peribronchitis subsided rapidly and sometimes dramatically, but more slowly in lung abscess and purulent bronchiolitis.

Penicillin administered in 15,000 unit doses intramuscularly every 3 hours was detected in the sputum in only 10 of 36 instances. Significant amounts of the drug were found in the majority of sputum samples from cases of lobar pneumonia but in lung abscess, chronic bronchitis and bronchiectasis the intramuscular route proved disappointing.

Penicillin has accordingly been administered by inhalation in single doses ranging from 15,000 to 100,000 units. Before each period of inhalation, patients who can profit by postural drainage are drained for 15 minutes, and all patients are asked to clear their chests as

far as possible Patients with definite bronchial spasm are given an antispasmodic Periods of inhalation last 15 minutes every 4 hours A mouthpiece proved more satisfactory than a face mask Thirty per cent glycerin has been used as a solvent since it provides a more enduring mist Care is needed in the choice of a batch of glycerin which has a neutral of pH and does not inactivate penicillin Oxygen may be used to volatilize the penicillin

The effect most easily studied has been on the bacterial content of the sputum Notable features are the rapid disappearance of gram-positive cocci and the appearance of coliform bacilli in nearly all sputa After 4 days pneumococci, streptococci, and staphylococci had disappeared from the sputa of all except 3 patients, and in these there was usually an obvious reason for persistence, such as continued breaking down of a loculated or multiple lung abscess Staphylococci disappeared within 2 days in 2 cases of purulent bronchiolitis which had not improved clinically nor shown any change in bacteriology of the sputum after 5 and 7 days on intramuscular penicillin (120,000 units a day), and in one of which the infecting *Staph aureus* was 6 times as resistant to penicillin as was the standard strain

Subsequent studies have in general confirmed these early observations, but have revealed further cases in which sputa containing organisms resistant to penicillin have remained* unaffected by the treatment They include *B proteus*, *Ps pyocyanea*, and resistant strains of *H influenza* and *H para-influenza*

Patients said that their cough became easier and less frequent within 1 or 2 days of starting treatment This disease was their treatment relief In most cases the sputum gradually diminished in amount and became mucoid instead of purulent

Recurrence of acute infections within 3 weeks of discharge during the period of cold weather followed in 2 patients before treatment was continued as outpatients with the hand inhaler Further work is required to decide how far continued treatment is necessary, but in view of a tendency to early relapse, shown by patients with bronchiectasis particularly, we have continued outpatient treatment in certain cases for periods upto 3 months

We feel satisfied that penicillin inhalation as administered has proved its value in 2 types of cases particularly chronic bronchitis with spasm (with or without acute exacerbation), and congestive cardiac failure brought on or made worse by respiratory infections Patients with pneumonia whose general lung infection has been improved by systematic chemotherapy but who were left with a relatively intractable bronchitis and peribronchitis were also speeded in recovery Similarly, patients with pulmonary tuberculosis (not included in the table) whose cough was aggravated by superadded non-tuberculous bronchitis were much relieved of their most troublesome symptom, without any ill effect upon the underlying tuberculosis being apparent Most patients with bronchiectasis were benefited, but in nearly all the sputum was not abolished It remains to be seen whether streptomycin given by inhalation would be more success-

ful by eliminating the infection with coliform and other penicillin-resistant organisms. The rapid improvement noted in some patients may be due in part to psychological reasons—for administration of a mist has a straightforward commonsense appeal to them and—in certain cases the frequent postural drainage and deeper respirations during treatment have also played their part. But the most telling argument is the change in quantity, quality, and bacterial content of the sputum.

Certain considerations have always to be remembered. First, there are patients with bronchiectasis, etc., whose infecting organisms are insensitive to penicillin even at the high concentrations obtainable locally by inhalation. We have met 8 such, since this study was made, and they showed no response to treatment either clinically or bacteriologically. Secondly, as the necropsies showed, in the early days at any rate, the sputum may be free from pyogenic cocci, and yet these cocci can be found in the infected small bronchi. It is not justifiable to assume that inhaled penicillin will diffuse through the secretions to the infected surfaces, unless the amount of secretion is kept down by adequate removal (either by coughing or by postural drainage). Neither can penicillin inhalation be discontinued solely on the evidence that a single sputum sample contains no pyogenic cocci, but rather must the clinical condition and the evidence of successive sputum examinations be taken into account. None of our cases was treated for less than 5 days, and most required considerably longer if early relapse was to be prevented. Outpatient treatment has numerous technical snags, but the work described here demonstrates that treatment can be begun or continued in this way, with the result that patients have been able to leave hospital sooner.

It is difficult to say yet whether any permanent improvement is likely to be effected by continued or repeated treatment of long standing cases of chronic bronchitis with emphysema or of bronchiectasis. The persistence of mucoid sputum is bound up with the structure of the chronically inflamed bronchi and bronchioles. They are usually lined with a complete epithelium, and the walls contain numerous mucin-secreting glands. Beneath the epithelium is a layer, more or less thick, of fibrous tissue which is highly vascular and infiltrated chiefly with plasma cells and lymphocytes. It would be very optimistic to suppose that such glands will regress, or that an epithelised cavity will alter much, even though pyogenic infection be permanently staved off and no further fibrosis take place.

In our view treatment with inhaled penicillin alone may speed up a permanent cure in lung abscess, purulent bronchiolitis, etc., which have not become chronic, but in the really chronic conditions it will arrest acute (and sometimes fatal) exacerbations and prevent the steady deterioration which each winter season brings. As a preoperative and post-operative treatment for lobectomy, however, or when a patient with a known bronchiectasis or chronic bronchitis has to undergo an abdominal operation, penicillin inhalation has many advantages.

Book Reviews and Notices

PENICILLIN THERAPY including **STREPTOMYCIN, TYROTHRICIN AND OTHER ANTIBIOTIC THERAPY** by **JOHN A. KOLMER** Second Edition, 1947 Appleton-Century Company New York and London XXIV+339 pages, 27 illustrations 25x17 cm, \$ 6 00

Kolmer's Penicillin Therapy first appeared in 1945 as a clinical guide to practitioners. Rapid advances in our knowledge of antibiotics has made it necessary to publish this second edition which is heavily revised, largely rewritten and considerably enlarged to include a great deal of new material and additional illustrations.

The book is written largely from the clinical standpoint, yet laboratory procedures are given in considerable detail to enable clinical pathologists to conduct assays of the serum, urine, spinal fluid and other materials as well as susceptibility tests of organisms to penicillin and streptomycin.

After a brief introductory chapter on chemotherapeutic compounds of biologic origin (antibiotics), the book is divided in three parts. The first part deals in six chapters, with history, production, assaying and properties of penicillin. Part two deals exhaustively with clinical applications of penicillin therapy in 16 chapters. In the first edition the clinical application of penicillin and other antibiotics in the treatment of various diseases were discussed from the standpoint of their etiological classifications. In this edition the clinical applications of penicillin, streptomycin, and other antibiotics are discussed under disease entities since so many diseases are caused by more than one pathogenic organism. This practical approach makes the book of maximum value to clinicians. The chapter on administration and dosage of penicillin gives full details of different methods, intravenous, intramedullary (bone marrow), intra-arterial, intramuscular, subcutaneous, use in cavities, topical and oral and evaluates their relative merits. The use of penicillin in pea-nut-oil and beeswax, in water-in-oil emulsions, in ointments, in powders, in troches, in tablets or in inhalations is fully discussed. Full chapters, with extensive references, are given to penicillin in the treatment of (1) septicemias, (2) subacute bacterial endocarditis and pericarditis, (3) suppurative brain abscess, and wounds of the brain, (4) diseases of the eye, (5) diseases of the ear, nose and throat, (6) diseases of the lung and pleura, (7) gonorrhea and genito-urinary diseases, (8) syphilis and other spirochetal diseases, (9) skin diseases, (10) wounds, burns and other surgical diseases, (11) bone and joint diseases, (12) miscellaneous diseases, (13) dentistry and oral surgery, and (14) antibiotic therapy in veterinary practice. The third part deals with Streptomycin, which has definitely established its value in clinical practice, and other antibiotics such as Tyrothricin (gramicidin and tyrocidine), Streptothricin, and others.

The general standard of the book is throughout high, the references to the literature are full and critical, and we have nothing but

praise for this immensely practical book, which must be on the desk of every practitioner,—general, physician, surgeon, eye, ear-nose-throat, skin, venereal, dental or veterinary specialist, who wishes to use these new chemotherapeutic agents rationally for the benefit of his patients. Altogether an admirable and comprehensive production!

PENICILLIN ITS PRACTICAL APPLICATIONS Under the General Editorship of Prof SIR ALEXANDER FLEMING First Ed 1946 Butterworth & Co., London, and Bombay XII+380 pages, 59 illustrations 22x14 cm Rs 24/8

The introduction of Penicillin in clinical medicine is perhaps the greatest recent advance in the history of therapeutics. Alexander Fleming who first gave the name Penicillin in 1929 to an antibacterial substance produced by a mould of the genus *Penicillin* has gathered round him some 27 specialists who are giving their experiences and possibilities of the clinical application of penicillin in the treatment of different diseases. The book is divided in two parts, general and clinical. In the general part, two chapters (1) on history and development of penicillin, and (2) on bacteriological control of penicillin therapy, are written by Fleming himself. The others deal with chemistry and manufacture (Bacharach and Hems), Pharmacy (Berry), Pharmacology (L P Garrod), and Methods of Administration (Hughes). In the second part which is purely clinical, are chapters on various diseases, medical, surgical, and special including dental and animal diseases, written by specialists in their subjects. The last chapter is devoted to penicillin and the general practitioner. The information supplied is accurate, there are selected references at the end of each chapter, and one may describe the book as a reliable British guide to the use of penicillin in daily practice. Of course, since the book was written some three years ago, there have been many additions to our knowledge of penicillin therapy, which the reader will have to supplement from the current literature.

PENICILLIN IN V D by K D LAHIRI, First Ed 1947 Himalaya Publications, Patna 108 pages, 17x10 cm Rs 5/-

This little booklet of some 100 pages is poorly produced and highly priced. Though foreworded by B Narayan, Principal, Patna Medical College, and introduced by Prof B N Prasad, Prof of Pharmacology, Patna Medical College, we fail to see how it will help the specialist in V.D for whom it is meant. The treatment of the subject is superficial, sketchy, and lacks balance and perspective and we do not think it is likely to guide anybody who is in a position to refer to books of Kolmer or Fleming reviewed above. We feel it is time our Indian writers of medical books and articles took themselves more seriously, there can be no excuse for books which are slovenly written and badly produced.

VITAMINS IN HEALTH AND DISEASE by J R. GOYAL, 1st Edition, 1947 Published by the author, P O Box 160 Delhi. 166 pages 18x12 cm Rs 5/-

In preparing this little book Dr Goyal has kept the general practitioner in mind and has rigidly confined himself to the practical aspects of diagnosis and treatment of disorders in which clinical use of vitamins has proved of value, reference to the physiology and pathology being brief. Wherever possible the vitamin content of Indian

articles of food is given Dr Goyal rightly draws attention to the fact that vitamins are chemical bodies having pharmacological action, and as such likely to produce toxic or untoward symptoms if used injudiciously. The information collected in this book is quite reliable and this brief presentation of known facts about vitamins is likely to be of help to the busy general practitioner who has no time to go through the vast literature or read larger treatises on the subject. The printing and get up are poor, surely the printers in Delhi can do better!

PEDIATRICS 1946 YEAR BOOK—Edited by J A ABT and A F ABT 1947 The Year Book Publishers, Chicago 464 pages, 18x12 cm \$ 3 75

The 1946 year book of pediatrics maintains the usual excellence associated with the well-known series of Year Books in different specialties published from Chicago. To the students, specialists and practitioners interested in diseases of children the year book of pediatrics brings an account of advances in diagnosis and treatment of diseases of children, abstracted with critical notes from the journals of different countries, regular perusal of which will make the reader acquainted with all the new advances in the speciality and the practitioner is certain to pick out many hints useful in the management of sick children. Articles appearing in the *Indian Journal of Pediatrics* and the *Indian Physician* also find place in this series. We may draw special attention of our readers to the articles on metabolic disorders of cystine, lipid, galactose, glycogen and glucose. Articles on jaundice, congenital biliary cirrhosis, epidemic hepatitis terminating in acute yellow atrophy of liver or hepatic sufficiency in biliary cirrhosis are of special interest in our country where infantile biliary cirrhosis with hepatic insufficiency is so common. Coeliac syndrome is also common in India and the dietetic therapy suggested by Anderson may with some modifications be adopted here. Powdered stomach is recommended in the treatment of fatty liver and other manifestations of infantile pellagra.

ELEMENTS OF SURGERY by FAUSET WELSH 1st Ed 1947 Oxford University Press, London, VIII+83 pages. 19x12 cm. Sh 7/6

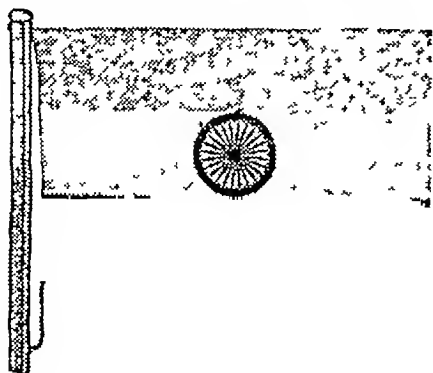
It was a good idea of Welsh to get his notes of routine surgical lectures to nurses at various Birmingham hospitals printed for a wider circle of readers. As it is the elements that matter in any science, a nurse or a medical student who reads this book will find all the essentials of the art and science of surgery presented here in a very readable form. The surgical dresser just entering the hospital wards who masters these brief 80 pages will have a sound foundation on which he can build a surgical superstructure later on.

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Clinical medicine cannot be practised divorced from ethics, sociology, and politics, nor can it altogether avoid metaphysics and philosophy without peril to its very existence. The Indian Physician has upto now scrupulously avoided mention of social turmoil or political changes, but now it cannot let go the *fifteenth of August 1947* in silence. The day is a red letter day in the history of India and also in the history of Great Britain. A powerful empire has voluntarily got off the back of the teeming millions, enslaved for over a hundred and fifty years. Whatever the circumstances which induced Great Britain to do it, nothing can detract from the glory she has won in this great act of granting liberty to a subject people, honourable alike in the freedom she gave and in the honour she preserved. It is a red letter day in the chequered history of Mother India. It is a glorious day of triumph for that selfless Architect of Modern India, who has been the virtual Master of India since 1919, that lonely pilgrim of Noakhali who has chosen to throw his lot with his people in the seceding new state of Pakistan. 1757 to 1947 is a brief interlude in the long life of old Mother India, who has seen many changes in her long life and has always contrived to preserve her culture in tact.

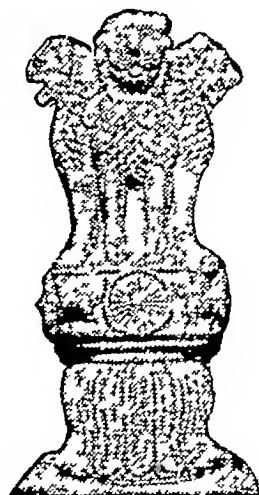
What of the future? The going of the foreigner has created a number of intricate new problems for India but she will triumph through them all if her children united through self-

sacrifice and discipline will remain loyal to her new Flag and Seal. Fifteenth of August 1947 is only the beginning of India's Battle for Freedom. She has still to free herself from a number of tyrannies and win her religious, economic, and political freedom. Tyranny is not easily conquered, yet we have this consolation with us, that the harder the conflict the more glorious the triumph. What we obtain too cheap, we esteem too lightly. It would be strange indeed if so celestial an article as freedom should not be highly rated.

What of the future of scientific medicine in New India? It is a plant of foreign growth and unfortunately has not yet taken deep root in its new habitat and its malnourished anaemic existence is a little threatened by the overgrowth of weeds, some ancient, some new. But we have faith that the modern scientific medicine is a hardy plant of healthy stock and its growth will languish or wither away only if its nurturing basic sciences of physics, chemistry, or biology disappear from India, and only if it fails to satisfy the social needs of the people.

Not a grave of the murder'd for freedom but grows seed for freedom,
in its turn to bear seed,
Which the winds carry afar and re-sow, and the rains and the
snows nourish
Liberty, let others despair of you—I never despair of you

Walt Whitman



Original Contributions

TRILENE ANALGESIA IN LABOUR

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Various means have been used from time to time for the relief of pain of a parturient woman. The very fact that newer methods and drugs are being suggested and tried, indicates that none of them so far utilised, is thoroughly satisfactory and can be used as the only means for a routine use. However, as one studies the advantages as well as the disadvantages of these various methods, one can select any of them, suitable to the individual case in question or better still a combination of more than one, so as to get the best result and what is much more important to give a thorough satisfaction to the patient from the point of view of relief of her pain during her confinement.

Arguments are often put forward that pain relief during labour is not an essential thing, as labour is a physiological process, nay, even quotations are given from religious books deprecating its use. Warnings are often given about the ill effects it is likely to produce on the child and the complications that may arise in the course of labour by the use of such unnatural means. The latter argument was, in fact, often put forward against the use of anaesthesia during surgical operations some 100 years ago. Do we not find that anaesthesia during any surgical procedure or an operation has become a routine procedure, nay, no patient will be willing to undergo an operation without it being given? The change in the attitude has resulted from marked improvements in the administration of anaesthesia and the safety offered to the patient's life under its effects. The same problem is now gradually appearing in non-connection with the relief of pain during labour. As more and more systematic investigations are carried out of the various means that could be utilised for the relief of pain during labour, it will be easier for the obstetricians to suggest the right type of analgesia during labour whenever a patient insists on its use.

Relief of pain during labour is not a new problem and it has been tackled from time to time by available analgesic drugs, in vogue during the various epochs in the history of obstetrics. The internal administration of drinks and drugs like alcohol, wines, opium, etc., was first used to the degrees of complete intoxication and after the introduction of chloroform and other inhalation analgesias were introduced in the obstetric practice. In the beginning of the present century the injection treatment with Morphia and Scopolamin, the famous German Twilight Sleep (Dammerschlaf) was suggested by

A paper read before the 67th Meeting of the Seth G S Med College and K. E. M. Hospital Staff Society on February 8, 1947 with Dr M N Desai in the chair

Prof Games Drugs like Paraldehyde and others were also used per rectum and as the analgesic and amnesiac properties of Barbiturates were discovered, oral administration of these drugs was tried and in the recent years their intravenous use was also made. Inhalation of Nitrous Oxide Gas for painless labour became popular by the construction of a portable apparatus by Minnitt and the method was further made popular by investigations carried out by the British College of Obstetrics and Gynaecology in gas-and-air and in gas-and-oxygen analgesia during labour, which can safely be used by the midwives. 10 years ago advances were made in local and spinal anaesthesia and it is no wonder that obstetricians also utilise these methods for the relief of labour pain and for operative deliveries. The Caudal Anaesthesia and continuous Caudal Analgesia have been popularised by the Americans and are being used on a large scale in various American Clinics. More recently 0.3—0.5 per cent Novocaine solution is being tried in America intravenously for painless labour. The effects lasting for 5-6 hours and in Russia 60 Mg of Vitamin B was used for painless labour by repeated intramuscular injection method with quite a promising result. During the war time Trilene was used as a short inhalation anaesthesia on field surgery and because of its comparative cheapness and easy mode of self-administration, like Nitrous Oxide, it has been suggested in the obstetric practice.

According to Hewer Trichlorethelene is the most potent and rapid analgesia of all the volatile chemicals including Nitrous Oxide. The credit goes to J. Ealm for calling attention to its use in Midwifery in 1942 for it appeared to have very little effect on the uterine muscle in patients in whom he had used it as an anaesthetic agent. He first suggested that weak mixture of Trilene and air would give an analgesia similar to that obtained with gas and oxygen. Freedman was the first to report the results of Trilene analgesia in 190 delivery cases by December, 1943 and he improvised the special inhaler bottle with breathing mask directly attached to it. The same year Edwards reported the results of 50 cases from his domiciliary practice using a slight modification of Marrett apparatus and calculated that on an average one patient requires 6 pence worth of Trilene. In 1945 Cairns reported results in 85 cases and DeBitt in 50 cases. The latter suggested further modification of Marrett's apparatus. Very recently in July, 1936, Barratt and Platts reported the results in 22 cases. Thus it will be evident that so far many papers have appeared on Trilene Anaesthesia and its complications, but few papers have appeared on the use of Trilene as an analgesic agent in Obstetric practice and in none of the papers except that of Freedmanns and Cairns, has the problem been approached from various aspects of obstetric importance.

I had the opportunity to make use of Trilene in a short series of 100 labour cases. I thought it advisable to report the results and at the same time invite suggestions and criticisms in the course of

discussion which will guide me from various aspects in modifying the technique in my further investigations

Methods of Administering Trilene - The Trilene is administered by Inhalation Method. A special bottle devised by Freedmann is very useful in that it does not allow the liquid to be aspirated even if the bottle is tilted. The patient used the same mask, as the Minnitt's Apparatus and breathes through it. The inspired and expired air moves to and fro at the top of the Freedmann's bottle and carries away Trilene vapour along with it. By this method only 0.65 per cent Trilene can be administered and there is no possibility of overdosing the patient. The patient is brought to the stage of Analgesia and may become slightly dizzy. At this stage the patient's index finger blocking the outlet on the face mask automatically falls aside or the patient herself allows the mask to drop from her face. Sometimes the mask is not sufficiently tightly held on the face and there is a good deal of leakage taking place from the sides so that the patient does not get adequate Trilene vapour. The patient must breathe in and out sufficiently deep to get any trace of Trilene. Trilene itself does not evaporate so easily as other. Freedmann had originally connected the mask directly to the top of the bottle and as there is every possibility of the patient dropping the bottle on the floor and breaking it either as a result of coming under the effect of Trilene or if the patient is non-co-operative and fails to take inhaled gas as instructed and becomes a little bit rowdy at the height of pain. A little modification of this arrangement by using a connecting rubber tube from the top of the bottle to the hand mask facilitates the bottle to be fitted to the side of the delivery table and the mask alone is then laid in the hand of a parturient woman. The length of this corrugated rubber tubing should not be however too long otherwise the inspired and expired air will not rush to the top of the Friedmann's bottle with sufficient force.

Firth and Stuckey have concluded from their study of decomposition of Trilene in close circuit anaesthesia that Trilene undergoes decomposition in the presence of Soda lime producing among other substances Dichloroacetylene and Phosgene. This decomposition occurs at room temperature but greatly increases as temperature rises. The presence of moisture affects the decomposition products. Trilene should on no account be used as an anaesthetic in the presence of any alkaline carbon dioxide absorbant. Hence Trilene should not be used in a close circuit apparatus as dangerous by-products e.g. poisonous and inflammable Chloroacetylenes which produce nerve palsies will be produced as the vapour passes through the warm soda lime canister. Trilene vapour is non-inflammable when mixed in any proportion of air at ordinary temperature, but when mixed with oxygen at temperature higher than 78°F inflammable mixture may be produced. Hence Trilene with oxygen should not be used in the vicinity of open flame, though Trilene air can be safely used.

The apparatus used is actually a simple one and occupies only a very small space in the obstetrician's bag and hence is not cumbersome. Moreover the amount of Trilene that may be required in each case as will be noted from the averages I have found out in my series is very small so that if the bottle is filled to its utmost capacity upto 1 oz it is more than sufficient for even a protracted labour case. There is no need for carrying heavy Nitrous Oxide and Oxygen cylinders. The initial and refilling cost of each in the present state of supply is still prohibitive in the use of this gas as a routine in any general hospital. On an average roughly 2-3 drams of Trilene are sufficient for analgesia for one hour and a dram of Trilene is sufficient for any multipara and double the amount for a primipara and the cost of each comes hardly to 2 to 3 annas respectively. Compared to it Nitrous Oxide in our country would require Rs 2 to Rs 3 per patient.

The only objection that is sometimes raised by the patient is that the Trilene gas has got a peculiar odour like the smell of fresh rubber goods, but after breathing for a few moments the patient can easily get over this peculiar sensation, particularly when she finds that there is complete relief of her pain during uterine contractions and actually demands inhalation in case it is stopped momentarily and the patient is allowed to experience pains without gas. Some patients particularly the multiparas who had never had occasion to make use of this gas during previous confinements are likely to be upset a bit when the mask is given for inhalation. They feel as if something abnormal has occurred and that is why there is need for inhalation of this 'anaesthesia'. If the patient is informed of the use of the gas during her ante-natal visits or given assurance at the time of admission for confinement, this difficulty can be easily got over. The patient should be instructed to hold the mask tightly against the face and the breathing of the gas should be started well in advance of the actual peak of pain so that she can even be instructed to bear down by holding the breath once the effect of analgesia is well established. If this procedure is tried the progress of the labour is not at all delayed, as a matter of fact patient can bear down more forcibly than before because of the analgesic effects produced by inhalation. The Trilene has no direct effect on the uterine contractions and hence the delivery is not at all protracted by its use. Even though the gas has got a peculiar smell it does not lead to any nausea and in spite of prolonged administration and even if the patient becomes deep in analgesia Vomiting reflex is not started when the patient comes out of it. Relief of pain prevents exhaustion of the patient and also minimises the associated surgical shock of labour, and on the whole patients are more fresh after confinement with Trilene than without it. One must admit that as compared to Spinal Analgesia the patient is left with a tendency to rest and sleep after confinement for a few hours which is also beneficial from the patient's point of view. As the gas is taken in a minimum concentration there is no possibility of reaching a

second stage of anaesthesia which is indicated in the case of Trilene by flushing of the face, slight tremors in the extrimities and disorientations of time and space and the patient having sensations of some dreams. This stage is never reached in Trilene Analgesia and the patient within a few seconds comes to herself as soon as the breathing is stopped from the mask. As stated above, Trilene has no effect on the uterine contractions nor does it produce any alteration in the blood pressure reading as was noted in my series. Blood pressure was taken in every patient before starting analgesia in between the pains and as soon as the child was born, before the actual separation of placenta had started so as to avoid fall of blood pressure produced by the post-partum haemorrhage. Trilene gas is practically non-irritant to the mucosa in spite of prolonged inhalation. Actual pharyngitis was noted in only one case of my series and bronchitis and coryza were absent following its administration. This observation was also made by Bose and Mukerji during their investigations on the use of Trilene as an anaesthetic agent during the experimental study on laboratory animals and reported in *Journal of Indian Medical Research*. They have proved experimentally that Trilene vapour did not have as much irritant effects on the respiratory passages as other. No excessive salivation or secretion of mucosa were noted by them. Trilene vapour however proved to be irritant to the eyes of the anaesthetised animals and good deal of lacrymation and congestion of the conjunctiva were produced though no true conjunctivitis was observed.

No bad effects were noted on the secretion of urine and Trilene was used even in cases of toxæmias and severe anaemias of pregnancy results of which will be discussed in detail later. So far no case of liver and kidney damage has been reported in the literature following the use of Trilene as an analgesic in midwifery. Taylor has reported from his experiments the absence of liver and kidney damage in prolonged exposure to Trilene vapour. This is out expected and supported by the work of Mr Kulkarni carried out in the Haffkine Institute and published in the *Indian Journal of Research*. During his study on the rate of disappearance of Trihalogen volatile Anaesthetics from blood after their administration as anaesthetics he has shown that the rate of disappearance of Trilene is practically double that of chloroform and figures lower than 2 mgs per 100 cc of blood being obtained within half an hour after the stoppage of anaesthesia. There is only one solitary case reported by Herdman in *British Medical Journal* in 1945 in which the patient developed acute Atrophy of liver following prolonged anaesthesia over 2 hours during which 2 ozs of the fluid was used. The patient had already a damaged liver as a result of septic deep wound with extensive burns. Bose and Mukerji produced bronchopneumonic and acute Focal Nephritic changes in animals by giving tonic doses of Trichlorethylene and Lande has also observed pathological changes in the kidney following prolonged administration of Trichlorethylene as an anaesthetic.

Bose and Mukerji however report that among the different samples of Trichlorethylene they have studied the more purified form, the Trilene seems to be the least toxic, the other samples showing 15 to 20 per cent greater toxicity than pure Trilene. It must however be realised that in toxæmia of pregnancy there is already kidney and liver damage to a varying degree and this problem will require a detailed study and further observations.

In my series Trilene was used for 100 consecutive cases without any special selection. As a rule no internal medication was used during the first stage of labour to avoid the effects of it and thus viciate the results of Trilene. Every patient was shown the method of inhalation and convinced that it was practically harmless and that there was nothing wrong as regards her delivery. She was asked to demand it as soon as she felt a bit uncomfortable with uterine pains. Before starting Trilene P. R. examination was carried out to note the degree of dilatation of the cervix. This need not be a routine procedure but was adopted as we wanted to study the effects of Trilene on the process of dilatation of the cervix. It was noted that in 84 cases gas was started after the cervix was fully dilated and in the remaining 16 when it was partially dilated. The amount of liquid required in each case and the total duration of analgesia were also noted down. As stated before the blood pressure and the urine of the patient were examined before Trilene was started and the blood pressure reading was taken again at the end of the second stage. The condition of the child was carefully noted at the time of the birth, particularly the degree of Asphyxia, Cyanosis and Apnea and the foetal heart rates were repeatedly taken in between the pains. Most of the inhalation anaesthetics like chloroforms, ether and nitrous oxide are followed by higher incidents of post-partum haemorrhage and hence this particular aspect was also investigated in the Trilene series. In most of the post-partum haemorrhage cases the condition could be easily tackled by just giving an injection of Pituitrin, Neogynergen or intravenous Ergometrin. In only one case was there the need of transfusion of the blood, but the occurrence of post-partum haemorrhage in that case cannot be attributed to Trilene, the patient being a multipara with twin delivery and with over distended uterus and requiring manual removal of the markedly adherent placenta. Soon after the confinement every patient was interviewed to find out whether she got relief of pain by taking Trilene and in a multipara whether she noted any difference between the previous confinements and the present one carried out under the effect of Trilene. The patients were grouped under various subheads like (1) thoroughly satisfied, (2) partially satisfied, (3) not satisfied. In the puerperium special attention was given to various conditions both in the mothers and the infants.

The following tables give details of findings during the present series —

Trilene was used at the time of confinements of 100 women, 33 of which were primiparas and 67 multiparas. No special selection of the cases was made but the analgesia was used as a routine for all the patients coming to the hospital for confinement. 61 patients out of 100 were thoroughly satisfied with the analgesia and had really painless labour. 34 had had partial relief and when asked if they would like to have the next confinement with or without Trilene all of them preferred to have it. 5 patients were not at all satisfied. This was because they were non-co-operative and would not carry out the instructions given, under the excuse that they felt suffocated by the gas. The other reason was that the duration was too short as they came later in labour. Respiratory complication of the nature of dryness and sore throat was noted in one patient only and slight bronchitis in another case.

TABLE I

	Primiparas 33 cases	Multiparas 67 cases	Total 100 cases
Satisfied thoroughly	18 54.5%	43 64.1%	61
Satisfied	13 39.4%	21 31.3%	34
Not satisfied	2 6.0%	3 4.4%	5

The table one gives the result of analgesia in 100 cases. The effects of Trilene were noted on the child from the point of view of incidence of still birth, asphyxia and the time taken for the first cry of the baby after the birth. For comparison the percentages of still births was obtained from 2,800 cases delivered during two years prior to the use of Trilene in labour. The results are given in Table No II.

TABLE II

	With trilene	Without trilene (2800 cases)	
			Out of the 99 babies 95 carried immediately while 4 took some time
Live birth	95%	95.7%	In the puerperium one child developed convulsions and one died of Atelectasis of the lungs on the second day of birth. This child was born marked asphyxiated and revived only after a good deal of efforts. Except these complications no other complications were noted in the children
Still birth	1%	4.3%	
Revived	4%	nil	

The effects of Trilene on the duration of labour also studied. No definite average figures can be derived due to the uncertain factor of the starting point of labour, but the general impression that one gets is that the administration of gas does not prolong the duration of labour. In this series of 100 cases only once the forceps had to be applied in a multipara, rest of them delivered naturally in spite of the fact the series included two face presentation cases, one breech with extended legs and one twin. The following table gives the nature of labours in comparison to the previous 2,800 cases.

TABLE III

	Trilene	Without Trilene	
Normal labour	04%	94 0%	No material difference in the occurrence of the perineal tear in the primiparas with or without Trilene. The multiparas however show definite lower incidence which may be explained by the fact that under the influence of Trilene the head to come out of the vulva very rapidly
Abnormal	6%	5 1%	the patient may not be able to overstrain and allow

TABLE IV

	Trilene Pri 33	Mul 67	No Trilene Pri 33	Mul 67	
P T	10	0	10	13	Even though there is very little difference in the actual incidence of perineal tear, the perineal tears were of smaller degree both in primiparas and multiparas. This can also be explained by the argument just stated.
No P T	14	58	14	54	

Post-partum haemorrhage — Before I discuss the problem of post-partum haemorrhage, let me make it clear on what standard I have grouped the cases of P P H. Usually there is such a wide variation in the actual quantity of blood loss during labour, that the quantity above 550 c.c. is taken as P.P.H. I have, however, not used that as a criterion but have grouped the cases under P.P.H. whenever there was a need for an injection of oxytocic drug to stop the bleeding as indicated clinically. By this method even slightly extra blood loss will be grouped under this heading and the same criterion was used to find the figures as control for comparison from 200 cases delivered just before Trilene series was started. This method is bound to give rise to high incidence of P.P.H. but so long as the same standard is maintained in the control figures the actual incidence of P.P.H. has only comparative value. Thus was noticed that 26 patients out of 100 had abnormal blood loss in the Trilene series as compared with 13 per cent cases in 200 control cases. As this is definitely an important complication of labour I would discuss this problem more in detail and try to find out if the study can help us in selecting the right type of cases for Trilene Analgesia and also in modifying the technique in order to reduce the incidence of P.P.H.

TABLE V

P P H		26% triene series		18% without Triene	
Primipara 31 2%		Multipara 24 1%		Primipara 20%	
				Multipara 18%	
Nor	Abnor	Nor	Abnor	Nor	Abnor
22 7%	50%	17 5%	32%	22 2%	20%
				180%	22 7%

The conclusions that one can derive by the study of the above table are —

1 The incidence of post-partum blood loss is definitely more with
Trelene than otherwise

2 On the whole the primiparas show comparatively more tendency towards excessive blood loss than Multiparas

3 In normal pregnancy both in primiparas and multiparas there are no greater chances of PPH with Tri-lene than without it

4 With pregnancy complicated by Anaemia, Toxaemia, Hydro-amnios, twins, etc there is higher incidence of PPH with Trilene Analgesia than without it

5 With abnormal pregnancy, particularly anaemic patients are more susceptible to P.P.H the incidence increasing directly with the severity of anaemia

6 The incidence of P.P.H was not however noted to the same extent in the Toxaemia group

Abnormal pregnancies	P P H incidence
Alight anaemia	40%
Severe anaemia	50%
Toxaemia of pregnancy	28.5%

7 The occurrence of P.P.H does not depend upon the amount of Trilene inhaled nor upon the duration of analgesia as will be seen from the following table —

Average duration of analgesia in hours	P P H		No P P H	
	Prim	Multi	Prim	Multi
	1.50	1.18	1.54	0.54

The following graph indicates the relationship between the percentage of cases and duration of the second stage of labour under the effect of Trilene. It will be evident from the graph that majority of the multiparas finished the second stage within 10 to 30 minutes while the primiparas within 30 to 60 minutes, which are the average figures even for normal deliveries without any analgesic drugs.

Thus it will be seen that even though Friedmann, the inventor of this apparatus, stated in his paper on Trilene Analgesia in labour in December 1943, that there seems to be no contra indications to its use, the present study of cases have brought out some of the definite contra indications for its use.

Trilene should be used with caution in

- 1 Primipara with protracted labour
- 2 Premature labour
- 3 Poly hydroamniotic
- 4 Pregnancy anaemia

Contra indication for its use—

The only contra indication from the point of view of the child is in premature delivery particularly in a primipara. The new born child is likely to be asphyxiated and is more prone to develop complications of intra cranial injury and haemorrhage. Prolonged administration of Trilene does seem to produce slight asphyxia though there is no difficulty in resuscitating the baby and the new born babies begin to cry immediately after the birth. But the colour of the child is slightly blueish as compared to the one delivered without any inhalation analgesia. The barbiturates, morphia and the inhalation anaesthesia definitely produce depression of the respiratory centres of the child and improper oxygenation. But among them Trilene seems to have the least action, barbiturates the midway and nitrous oxide the most. Apnea, however, is more prolonged in cases of morphia and barbiturates, while it is least with Trilene. Spinal anaesthesia seems to be the best from this point of view even though the child is slightly asphyxiated because of the powerful toxic contraction of the uterus,

it cries immediately after birth. Evidently the asphyxiated condition is seen more commonly in protracted labour cases or in cases of primiparas in whom the head is held up for a long time on the perineum. The patient cannot overstrain with force during the contraction when the inhalation of Trilene is carried on. At the same time there is less incidence of perineal tear after the use of Trilene. Taking all these facts into consideration and noting the results in these 100 cases one feels that a combination of Trilene and Epidural anaesthesia, which can be given about $\frac{3}{4}$ th of an hour before the expected delivery will be an ideal procedure in a primipara or a protracted labour case. In a multipara the process of labour is so hurried that inhalation with Trilene seems to be an ideal thing which can be started immediately after the admission of the patient if she is having strong labour pains. In such cases there is hardly any time for carrying out the Spinal Analgesia which requires at least 20 minutes for its complete action and the delivery of a multipara with strong labour pains may be finished even before that stage is reached. In a primipara, however, a combination of Trilene with spinal analgesia in the end would bring about relaxation of the perineum and less hamper the progress of the head so that there is less chance for favouring undue congestion of child's brain. The use of spinal analgesia in the end also improves the tone of the uterus and reduces the duration of the third stage and prevents post-partum haemorrhage. In a premature delivery again Trilene should be given next preference to spinal analgesia. As stated above, premature children are more prone to develop various complications and other manifestations of intra cranial haemorrhage and mild attacks of oedema of the lungs. There was no case of still birth in the series which can be attributed to the action of Trilene. The only still birth in the series was seen in a patient who had accidental haemorrhage with manifestations of toxæmia and pregnancy. The child born in this case was a premature, weighing about $4\frac{3}{4}$ lbs.

Though no investigations as regards prothrombin level of the new born child were carried out, the general impression that one gets after study of these cases is that in case of primipara the protracted labour itself may be responsible for manifestations of various haemorrhagic diseases of the new born. The incidence of these conditions was not more than in the series delivered without analgesias, so that its causation appears more in undue protraction of the labour rather than the use of Trilene itself. This does not apply in cases of painless deliveries under heavy doses of barbiturates. In those cases there is a definite drop in the prothrombin level and hence there is increased incidence of various haemorrhagic manifestations and jaundice in the new born by barbiturates amnesia. The prophylactic injection of vitamin K in a primipara may be given particularly if one expects somewhat protracted labour. There is no harm in giving Trilene even if there is slight cephalopelvic disproportion. The uterine pains are more painful in such cases and during the first and second stages of labour the Trilene can be used. Caudal injections should be

given only if the engaging diameter has passed the plain of pelvic obstruction so as to avoid unduly powerful contractions of the uterus and stretching and thinning out of the lower uterine segment

From the point of view of the mother there does not seem to be any special contra indication for the use of this gas except when the patient is suffering from severe anaemia of pregnancy or any respiratory disease at the time of labour. Evidently a person who is prone to develop slight cold on exposure or has unhealthy throat should not be given Trilene Analgesia. Since Trilene has no effect in raising blood pressure it can safely be used even in toxemia of pregnancy cases and here again combination of Trilene and Caudal analgesia in the end will be useful especially in cases of Eclampsia, spinal Analgesia will definitely lower the blood pressure, remove spasms of the renal vessels and thereby increase secretion of urine. As stated above, Trilene Analgesia has no direct injurious action both on liver and the kidneys.

It must be realised however that Trilene cannot be used for carrying out the repair of the perineal tear after confinement by using Friedman's apparatus, as it only produces a stage of analgesia and not anaesthesia. The use of Trilene for actual anaesthesia has no special advantage over other anaesthetic drugs and when there is need for an actual anaesthesia more safe methods both for the mother and the child can be used, for instance, local anaesthesia and caudal analgesia.

CONCLUSION

It will thus be realised that Trilene is a more suitable analgesia for a routine work and even for home confinement cases. It does not require any elaborate apparatus and technique in addition. It is quite safe to the mother and the child if contra indications given above are carefully observed. It does not affect the progress of labour and hence does not increase the operative incidence during the delivery. Since it can be self administered, an obstetrician can manage it, single handed.

Compared to it, a cumbersome apparatus may be required in the case of nitrous oxide gas or nitrous oxide air administration with suitable apparatus. That method is rather costly and the Cyanosis that is invariably produced by NO_2 may endanger the life of the new born. Anoxemia can produce permanent damage to the cortical cells of the brain of the anaesthetised, an injury which may result in nervous and mental sequela or even death. Montgomery in Philadelphia in his investigations found that Nitrous Oxide and Oxygen Anaesthesia during actual obstetric operation were responsible for the maternal death and even rupture of the uterus in nearly 25 per cent of cases of death. Chasler Moir in 1937 has devised an apparatus in which pure Nitrous Oxide was given. With this method he obtained good relief in 70 per cent cases and fair relief in 14 per cent cases, which is the maximum one can expect from Nitrous Oxide Analgesia with associated risks given above. In my series of 100 cases, 61 cases were thoroughly satisfied with the result, 34 patients were partially satis-

fied and 5 patients were not satisfied at all. The results can be improved by further experience in the method of administration and by combining it with drugs like Chloral Bromide and Demerol during the first stage of labour. However, the obstetrician must be prepared for complications of increased cyanosis of the baby etc with the use of these drugs. It will be interesting to note how the simultaneous administration of Vitamin B will help to improve the result. The investigation on these lines have already been started on the second series of 100 cases. I feel that the use of Trilene alone can be made a routine in multiparas and it can be used upto within an hour of delivery in a primipara case followed by a single injection of caudal analgesia, which will be ideal in avoiding all the complications. Thereby the difficulties and failures of the Caudal Analgesia caused by the improper development of the sacral arch, which is noted to be absent in 25 per cent of the cases, can be further reduced and the patient can be given better security and feeling of satisfaction in relief of labour pains. The dread of having to undergo a prolonged ordeal of pain at the time of labour will be removed and once this psychological inhibiting factor is got over, one should expect the corresponding disappearance of the most annoying obstetric complications, viz, spastic cervix, primary uterine inertia and uterine colics. The pregnant mothers, should no more look upon the labour ward as 'Chamber of Pangs' and could now walk in with more confidence and security for a painless normal delivery.

DISCUSSION

Dr K M Masani remarked that women wanted relief of pain during the first stage of labour and not during the second as advocated by the speaker. Moreover he added with Trilene analgesia as compared to Nitrous Oxide a higher incidence of P P H is observed.

Dr N F Saher suggested a minor alteration in the design of the apparatus in shifting the inspiratory valve to the angle piece on the face mask near the expiratory valve. This change he added would remove the objection of using a long breathing tube with its consequent risk of inhaling a high percentage of CO₂ and vitiating the concentration of Trilene.

Dr G S Ambardekar said that Trilene anaesthesia was unsafe because it did not produce sufficient relaxation and it produced tachynea due to sensitization of the nerve endings in the walls of the alveoli and capillaries thereby reducing the period of inspiration and expiration leading to the anoxia. He further remarked that there is a risk of explosion when Trilene concentration is over 10%.

Dr B V Aroskar asked the speaker how he would foresee that a case receiving Trilene analgesia would have a protracted labour. In his experience the incidence of P P H in pregnancy anaemia was not high but the cause of death was sepsis or heart failure.

Dr Purandare in reply said.—I must thank Dr Saher for the modification in the apparatus that he has suggested so as to avoid dead space produced in the corrugated rubber tubing. The transference of the inspiratory wall nearer the mouth piece will certainly help to get over the difficulty. Dr Ambardekar had stated that Trilene Oxygen mixture should contain over 10% Trilene before it can become inflammable. If this is so one can safely have an additional attachment on the mask through which oxygen can be given in larger concentration when the head is travelling on the perineum. Thereby oxygenation of the mother's blood and tone of the uterine muscles will be maintained and thus post partum haemorrhage in the mother and synoxia in the child can be got over. Dr Aroskar raised an objection to one of my contra indications viz. protracted labour and how to foresee it. But may I state that one can certainly stop Trilene when the labour is actually getting protracted and replace it by caudal analgesia. As a rule in anaemia of pregnancy incidence of post partum haemorrhage is less and as this study indicates abnormal high incidence of post-partum haemorrhage in the anaemia group this type of cases should not be given Trilene. I do not agree with his statement that it is not the abnormal pregnancy but the protracted labour responsible for post partum haemorrhage in these Trilene series because as will be known from the statistics that there were very few protracted labour cases in this group.

Critical Notes and Abstracts

PHARMACOLOGIC BASIS OF CARDIAC THERAPY HARRY GOLD (J.A.M.A. 1946 132 574)

Action of Digitalis in Failure—How digitalis acts to relieve heart failure has long been a matter of controversy. We now believe, however, that the primary mechanism consists of an increase in the force of cardiac systole as a result of direct action on the heart muscle. Most of the other significant changes in the heart and circulation which occur in patients with heart failure after digitalis follow as secondary adaptations.

Vagal and extravagal action of digitalis—Slowing of ventricular rate is one of the outstanding results of digitalis action in auricular fibrillation. Two mechanisms are involved. In some instances blocking the vagus by 2 mg of atropine sulphate intravenously abolishes the slowing while in others the atropine has little influence on the slowing. It has been found that in one and the same person the slowing may be vagal at one time and extravagal at another and further that the deciding factor is the dose of digitalis. As the dose is increased the control of the ventricular rate tends to pass from the vagal to the extravagal mechanism. It is important to note that in the operation of this adaptive mechanism the resting rate may remain unchanged.

Physical exercise to the limit of the patient's endurance has the same effect on rate as blocking the vagus with atropine. When slowing is by the vagal mechanism exercise may accelerate the rate to 180 a minute, but when the slowing is by the extravagal mechanism exercise rarely accelerates the rate above about 100 a minute. This is a matter of importance in the maintenance of patients with auricular fibrillation. In the treatment of these patients it is not uncommon to find digitalis reducing the rate from 140 to 70 when the patient is at rest. When he is up and about, however, he complains of palpitation and breathlessness. Free physical activity raises the rate to uncomfortable peaks when the mechanism of control is vagal. If larger doses of digitalis are given, the rate control passes to the extravagal mechanism, which prevents the exaggerated acceleration with exercise, even though the resting rate may not be materially lowered.

Single average full dose method of digitalization—The human assay of digitalin shows that 1 mg produces the same effect in men by oral administration as 1 Gm of the Standard Digitalis Powder. The same relationship is found to apply to the effects in auricular fibrillation. The fact that digitoxin is so potent and so well absorbed suggested the possibility of employing it in a single dose method of digitalization to replace the multiple dose methods employing digitalis leaf or the tincture. Our results indicate that the most favourable routine technic for digitalizing patients is to administer 1.2 mg

of digitoxin at one time. This produces a high degree of digitalization in a period of about 6 to 10 hours in the place of the 24 to 48 hour period required for the divided dose methods in which digitalis is used. One cannot use the digitalis leaf or the tincture by this method, because the equivalent amount of digitalis, namely 12 gm, will cause nausea or vomiting by local action in about 10 to 20 per cent of the cases. The therapeutic effects are maintained in the majority of cases by a single daily dose of a tablet of 0.2 mg. The use of digitoxin in this way has greatly simplified the problem of digitalization. Some patients need closer to 2 mg to digitalize them fully but from our experience with more than 1,000 single dose digitalizations with 1.2 mg a negligible number, about 2 out of 100, show nausea or vomiting. The safety of this method is therefore beyond question.

Average Dose—The most useful average dose from the clinical standpoint, is one which is likely to exert an effect close enough to the desired effect, in a high proportion of patients and with reasonable freedom from toxicity. In the case of digitalis, the significance of the term average dose is indicated by the following study. Two-tenths of a Gm of digitalis was given daily to 40 ambulant patients with auricular fibrillation. The desired effect was to maintain a rate of 70 a minute. When this dose was given to a large group of patients for a period of 4 weeks the rate was rarely exactly 70 a minute for any given patient, but a result sufficiently close to that was obtained in about 70 per cent of the group, namely a rate ranging between 60 and 90. The rest were either too tolerant and maintained rates up to 100 or faster or were so susceptible as to attain the rates of 40 or slower.

Quinidine—Quinidine is the most important agent we possess for abolishing many disorders of rhythm and for preventing their recurrence. Experiments show that its maximum absorption takes about 2 hours, so that the peak effect may be expected at that time and that most of the effect wears off in less than 24 hours. We have also found in experiments on man that a fixed daily dose shows cumulation for only 3 or 4 days, unlike digitalis in which a fixed daily dose may show cumulation over a period of 2 or 3 weeks. This signifies that any daily dosage level of quinidine which fails to produce the desired effect in 3 or 4 days is likely to fail to do so no matter how long it is continued. The method of giving quinidine which we apply in a case in which there is no urgency, is the administration of 5 gr 3 times daily, or 15 gr a day for 4 days. If the abnormal rhythm is not controlled, the dose is increased to 20 gr daily for 4 days. One continues to increase the dose by 5 gr daily for 4 days until a daily level is reached at which the abnormal rhythm goes or until minor toxic effects preclude its further use. If there is great urgency as in some cases of ventricular tachycardia, one builds the concentration more rapidly on the peak effect of each dose. In such a case we use 5 or 10 gr every 2 hours. By this method failures are few.

Mercurial diuretics—The tendency to overlook the principles of dosage which have gone far in establishing sound and effective digi-

tals therapy is particularly noteworthy in the current application of the mercurial diuretics in the treatment of heart failure. These materials, mercupurin, salyrgan with theophylline, and mercurhydrin, represent one of the most noteworthy advances in cardiac therapy in the last 25 years. Unfortunately only a small part of the potentialities of these drugs is exploited, since they are commonly reserved only for cases in which there is frank edema or pulmonary rales occur. It deserves emphasis that, in heart failure, edema may be present in the lungs and other tissues long before the usual clinical signs, namely rales and pitting of the legs, that shortness of breath on effort, cough and orthopnea are usually much earlier signs. Cardiac patients with these symptoms make up the largest group of potential beneficiaries of the mercurial diuretics. Furthermore, the common system of dosage calls for an injection not more often than once in 4 to 7 days, with discontinuance of the drug until edema reaccumulates. One should note that the organic mercurials are usually eliminated completely or almost so in less than 24 hours. A dose may therefore be repeated with safety every day. Indeed, in cases of advanced heart failure the results of the daily dose to abolish the failure, and of the maintenance dose at suitable intervals to prevent its recurrence, provide us with one of the most dramatic aspects of modern cardiac therapy.

THE NISULFAZOLE TREATMENT OF CHRONIC ULCERATIVE COLITIS RALPH H MAJOR (J. A. M. A. 1946 485-491)

With the appearance of sulfapyridine and sulfathiazole, the nitro analogues, 2-(p-nitrobenzenesulfonamido)-thiazole, were produced and their properties studied. The studies showed that these two compounds were not readily absorbed from the intestines, an observation which suggested their use in the intestinal infections. As the compound 2-(p-nitrobenzene-sulfonamido)-pyridine was less readily absorbed, its effects on a patient suffering with ulcerative colitis were studied with results so encouraging that we began a systematic study of its effects in chronic idiopathic ulcerative colitis. For purposes of simplification, 2-(p-nitrobenzene-sulfonamido)-pyridine was called Nisulfadine, and 2-(p-nitrobenzenesulfonamido)-thiazole was called Nisulfazole.

All of the cases treated were diagnosed chronic ulcerative colitis after proctoscopic examination showed the presence of ulcers and the x-ray showed the characteristic picture of "feathering" of the walls of the intestine, loss of haustration and the presence of the characteristic "gardenhose" type of colon. Our studies in this series of patients have added nothing to our concepts of the etiology of this disease.

The general treatment of the patients followed the lines usually recommended in the treatment of this disease. The patients were placed on a bland, residue-free diet and encouraged to partake freely of fluids. If the patient had lost much fluid from watery evacuations, subcutaneously normal saline infusions were administered. If the patient had very frequent stools, laudanum or paregoric was admin-

istered, and if they suffered from tenesmus, belladonna or trasantin was employed. Patients showing marked anaemia were given blood transfusions.

Nisulfazole was administered in the early cases only by mouth, either in tablets, capsules or enteric coated tablets. The enteric coated tablets were employed in patients who developed nausea, but often prove unsatisfactory as patients who had a very active diarrhea often passed these tablets undissolved. The initial dose by mouth varied from 4 to 6 Gm in 24 hours. If nausea developed, the drug was withdrawn for 24 hours and then medication was resumed with a dosage of 2 or 3 Gm daily.

Later the drug was administered by rectum in pectin suspension, two or three instillations of 10 cc of a 10 per cent suspension. This method of administration was equally effective and had the advantage of producing no nausea. While patients receiving nisulfazole only by mouth showed nisulfazole blood levels varying from 15 to 163 mg per 100 cc, patients who received the drug by rectum in the same dosage rarely showed more than a faint trace of nisulfazole in the blood. Thirty-four of the 37 cases "recovered" while three are markedly improved. By "recovery" we mean that the patients were symptom-free and not passing more than 2 or 3 normal appearing, well formed stools daily. That these patients were not all "well" is obvious from the fact that on dismissal the x-ray picture of the intestine still showed lack or diminution of the normal haustration and that ten of them subsequently suffered from relapses of varying degrees.

The causes of these relapses were not always clear. The most common cause assigned by the patients was dietary indiscretions. In two instances, however, relapse was accompanied by purulent maxillary sinusitis, in one patient by acute pyelitis and in one patient by erythema nodosum.

Some of the patients are still taking nisulfazole and some have taken it for a considerable period. One patient has taken nisulfazole in doses of 2 Gm daily for seventeen months, while another has taken it in the same dosage for 26 months, and several other patients have taken it for several months after leaving the hospital. We have not seen any untoward effects following such long administration but have insisted that such patients remain under continued observation so that frequent blood counts and urinalysis can be carried out.

In a disease such as chronic ulcerative colitis, a disease noteworthy for its chronicity and its tendency to recurrence, it would be hazardous to assert that most of these patients are permanently cured. We do feel, however, that therapy with nissulfazole has given us better results than any other treatment with which we are familiar.

THE SYSTEMATIC TREATMENT OF 227 CASES OF ARSENIC POISONING (ENCEPHALITIS, DERMATITIS, BLOOD DYSCRASIAS, JAUNDICE, FEVER) WITH 2, 3-DIMERCAPTOPROPANOL (BAL) H EAGLE and H J MAGNUSON (Jour of Syph Gono and Ven Dis 1946 420-441)

The compound 2, e-Dimercaptopropanol (BAL) was developed for the local decontamination and treatment of arsenical blister gas injuries. The material administered systematically proved effective in the treatment of various types of experimental arsenic poisoning, the detoxifying effect being due to the fact that it removes toxic arsenicals from an otherwise firm combination with tissues, with the excretion of the stable thioarsenite so formed.

Toxicity—As of May 8, 1944, reports had been received on a total of 61 patients with serious arsenic poisoning resulting from the intensive treatment of syphilis who were treated with a solution in peanut oil containing 5 per cent BAL and 10 per cent benzyl benzoate. In the majority of these, the maximum single dose of BAL was 150 mg, or approximately 25 mg per kg, repeated every 4 to 6 hours to a maximum of four doses during the first 24 hours. At that dosage level, less than 1 per cent of more than 700 injections was followed by minor and evanescent toxic reactions.

Although the therapeutic results were also reasonably satisfactory, the experimental data from this and other laboratories indicated that somewhat larger doses of BAL might be necessary for the effective treatment of poisoning caused by the arsenical blister gases. Accordingly, the effects of such large doses, up to a maximum of four doses of 5 mg per kg each given at four hour intervals, were studied in 60 patients of both sexes. With these larger dosages of 4 and 5 mg per kg, pain at the site of injection was common but was not appreciably greater than that occurring after other types of intramuscular medication. The other toxic manifestations, in order of decreasing frequency, included nausea, vomiting, and headache, a burning sensation of the lips, mouth, throat, and eyes, sometimes with accompanying lachrymation, rhinorrhea or salivation, generalized muscular aches, burning and tingling of the extremities, with sweating of the forehead and hands, pain in the teeth, and a sense of constriction in the chest, with a feeling of anxiety and general agitation. These symptoms tended to reach a maximum within 10 to 30 minutes after the injection and then subsided rapidly within 30 to 50 minutes of the injection.

Although these evanescent toxic reactions occurred in varying combination and in varying frequency, they were not significant in either number or severity until the 4 mg per kg level had been exceeded. One may conclude that the maximum dosage of BAL which

it is feasible to administer intramuscularly in man at four-hour intervals is 4 mg per kg in 4 injections, and smaller doses, on the order of 25 mg per kg, are desirable in order to minimize local pain and subjective reaction

Results in the systematic treatment of arsenic poisoning in man
Arsenical Encephalitis—Reports have been received on a total of 55 patients with toxic encephalopathy, usually resulting from intensive or semi-intensive treatment with mapharsen or its analogues and treated with BAL. All recovered completely, and in 14 of the 15 patients definite improvement was apparent within less than 24 hours after treatment with BAL was instituted

Arsenical Dermatitis As of June 1, 1945, reports had been submitted to this laboratory on 63 patients with arsenical dermatitis of varying severity treated with BAL. In contrast to the patients with encephalitis discussed in the preceding section, the average duration of arsenical treatment in these patients had often been measured in weeks rather than in days, more than one half were treated with neoarsphenamine rather than mapharsen

In the first 25 patients with mild cases, treatment with BAL was begun on an average of ten days after the development of the skin rash. Of these, 22 (88 per cent) recovered completely within 1½ to 5 days, averaging two days. The other three patients seemed unaffected by BAL in the dosage used

Of the first 38 patients with exfoliative dermatitis, BAL seemed to have definite therapeutic effect in 30 (79 per cent). Within 1 to 10 days after the administration BAL, averaging 3 days, the edematous inflammatory reaction of the skin lesions usually decreased, but the plainness exfoliation often progressed, and in some cases seemed actually to be accelerated as the inflammatory reaction subsided. Some of these patients were either well or were discharged from the hospital from 75 to 90 per cent recovered five days after the beginning of BAL therapy, and more than 75 per cent had recovered by the fifteenth day after discharge

Agranulocytosis In the 11 patients reported to this laboratory as of June 1, 1945, the duration of the complication prior to BAL therapy varied between 12 hours and 6 days (average, 2, 3 days). Nine of the patients had received intensive or semi-intensive treatment with mapharsen or clorarsen, averaging a total of 1,000 mg over a 21 day period, and most had received their last infection of arsenical one day before the onset of agranulocytosis and three days before the beginning of BAL therapy

An average total of 16 Gm of BAL was administered over a 5 day period and an average of 0.40 Gm during the first 24 hours. Ten of the 11 patients recovered so promptly as to suggest a possible casual relationship. The circulating polymorphonuclear leucocytes usually began to increase by the second day of treatment, and the total white blood cell count approached normal levels within 7 days

Jaundice Reports have been received on a total of 16 patients with jaundice occurring as a complication of arsenotherapy and

treated by intramuscular injections of BAL. The data suggest that BAL may perhaps accelerate recovery in a small proportion of patients with so-called postarsenical jaundice. The final evaluation of its therapeutic efficacy in this form of arsenic poisoning must await the study of a larger number of patients.

Massive overdose with Mapharsen—Four patients who were in effor given a single massive dose of mapharsen from 7 to 20 times the usual therapeutic dose of 60 mg have been treated with BAL, with a favourable outcome in those patients who received both prompt and adequate treatment. Thus a man weighing 57 kg received 600 mg of mapharsen instead of 60. This dose of 10.5 mg per kg kills the occasional dog or rabbit similarly injected. The patient immediately went into moderate shock, the pulse becoming thready and the respirations labored and asthmatic. Three cubic centimeters of a 5 per cent solution of BAL in peanut oil (150 mg = 26 mg per kilogram) were injected intramuscularly one-half hour later, whereupon symptoms disappeared in the following half hour. A total of 6 cc of the BAL solution were given on the first day, 9 cc each on the second and third days, and 6 cc on the fourth day. The total of 30 represents 1,500 mg of BAL, one-fifty of which was given within a period of 24 hours, of the arsenical.

Recommended method of Administration—The results in various types of arsenical poisoning treated with BAL indicate that in serious and rapidly progressing complications such as toxic encephalopathy, treatment should be initiated at the earliest possible moment and continued intensively for at least 48 hours. The frequency of injection may thereafter be reduced. Several patients with exfoliative dermatitis have relapsed when BAL was discontinued after from 4 to 8 days' treatment, and it is therefore suggested that the treatment of that complication be continued for a minimum of 10 days.

In the light of these considerations, the following regime of treatment is suggested: mild cases (Fever, rash, mild arsenical dermatitis).

(a) Unit Dose Per Injections of BAL—25 mg per kilogram. In a man weighing 60 kg, this represents 150 mg, or 15 cc of the 10 per cent solution.

(b) Frequency of Treatment. On the first two days, patients may be given four injections each day at four-hour intervals. Thereafter, the dosage may be reduced to one or two injections daily for ten days, or until complete recovery.

Severe Cases (Exfoliative dermatitis, toxic encephalopathy, blood dyscrasias, jaundice, massive injection of arsenical).

(a) Unit Dose Per Injection—3 mg per kilogram. In a man weighing 60 kilograms this represents 180 mg, of BAL, or 18 cc of the 10 per cent solution.

(b) Frequency of Treatment. Treatment should be repeated every 4 hours for the first 2 days, i.e. a total of 12 injections in 48 hours. Depending on the therapeutic response, treatment may there-

after be reduced to two injections daily for ten days, or until complete recovery

THE TREATMENT OF COMPLICATIONS OF ARSENO-THERAPY WITH BAL (BRITISH ANTI-LEWISITE) A B CARLETON, R 'A PETERS, L A STOCKEN, R H S THOMPSON and D I WILLIAMS (Joul of Cli Inv July 1946 497 527)

In recent years, progress in our knowledge of the intermediary metabolism of carbohydrates has led to more detailed information on the progressive steps by which the carbohydrates, glucose and glycogen, are broken down in cells to carbon dioxide and water. Each step is controlled by a definite enzyme. One of the penultimate stages of this degradation is pyruvic acid. In so far as tissues cells rely upon carbohydrates for their energy, the stages in breakdown are all of importance. It follows that one way of interfering with cell life is to interrupt the activity of some enzyme essential to tissue carbohydrate metabolism.

Some years ago it was realized that the poisons, iodoacetic acid and dichloroethyl sulphone, which can induce pathologic change in skin, have a selective inhibitory action on the pyruvate oxidase enzyme system. It was further known before the war that arsenite too interferes with the metabolism of pyruvic acid and that pyruvate oxidase system contains a component sensitive to very small concentrations of arsenite, which also act selectively on it at these levels. It follows that the metabolism of carbohydrate is poisoned at an important stage by traces of an arsenical.

On the basis of these facts, it is logical to use the pyruvate oxidase system as a test for new antidotes against arsenic, and during the war a research upon these lines was initiated. As a result of the systematic attack made on this problem from the biochemical angle, it was found that simple 1,2-dithiols (of which BAL $\text{CH}_2\text{SH}-\text{CH}_2\text{SH}-\text{CH}_2\text{OH}$, is an example) are capable both of exerting a marked antidotal action against the poisoning of this enzyme system by trivalent arsenicals, and, more important still, of reversing this poisoning when once established. These effects are brought about through the ability of 1,2-dithiols to form stable ring compounds with trivalent arsenicals.

Since experimental work on animals indicated the value of this drug in the treatment of toxic manifestations of arsenicals, it seemed desirable to continue this study in man. Accordingly 30 patients with acute exfoliative dermatitis secondary to arsenicals were treated with BAL. Twenty-one cases received the drug intramuscularly as 5 per cent solution of BAL in 10 per cent benzyl benzoate in peanut oil. The total dosage given varied from case to case according to the condition of the patient, but usually consisted of a course of 2 ml given by deep intramuscular injection into the gluteal region twice daily for 3 or 4 days, followed by a further course, if no obvious improvement occurred, of it, at any time, there were signs of any relapse in the condition of the skin. Nine cases were treated by injection.

Eighteen of the 21 cases treated by injection were severe or moderately severe, weeping or desquamation or exfoliation from the affected areas. Two of the cases ended fatally. Case No 6 died suddenly after mild rigors, and at autopsy showed a dermal bronchopneumonia, while Case No 15 developed a sloughing glossitis, stomatitis and pharyngitis and an early granulocytopenia. In sixteen of the 18 cases the number of days from the first injection of BAL to the time when the skin became "normal" or "almost normal" was as follows: 273 days for those followed through to "normal" and 189 days for those in which an "almost normal" report was received. Improvement was noted in from 2 to 19 days after onset of treatment. There seemed to be a definite tendency in more than 1 case for a rapid cessation of the oozing, followed by a more intractable persistence of the erythema.

Several cases also showed evidence of relapse. This can be explained if "arsenic" from some other part of the body enters the blood stream and again poisons the skin. From our experience, good results have followed a second course of injection of BAL.

It is realized that the number of cases available for this report is too small to eliminate the possibility of serious statistical error in the interpretation of the results. On the other hand, the striking clinical effect in some of the cases, and the apparent reduction in the time of healing warrants a more extended trial of this new compound. The experimental evidence obtained from animals further supports this contention.

BAL IN ACUTE MERCURY POISONING W T LONCOPE and JOHN A. LEUTSCHER (Joul of Clin Invest July 1946 557-567)

The extensive investigations upon the mechanism by which arsenic poisons the protoplasm of cells and the discovery that the di-thiol 2,3-dimercaptopropanol or BAL (British Anti-Lewisite), possesses an avidity for Lewisite and trivalent arsenicals, thus sparing injury to the cells and their essential enzymes led to the suggestion that the toxic action of other metals might be explained in a similar manner. Evidence is now at hand to show that the principles involved in the injurious effect produced by mercury and cadmium are analogous to those ascribed to arsenic.

It has been generally stated that a dose of 0.5 Gm of mercury bichloride by mouth is rarely, if ever fatal, that when 10 Gm is swallowed and vomiting does occur within 10 minutes, the prognosis is poor, and that 15 Gm often results in death.

Twenty-three cases of acute poisoning by mercury bichloride have been treated with intramuscular injections of BAL. Eight of these patients swallowed not more than 0.5 Gm of mercury bichloride, and treatment with BAL was started from 20 minutes to 3-1/2 hours later. All made a prompt recovery.

Six patients swallowed 10 gm. Five were treated within 1 to 3-1/2 hours, all recovered within 2 to 8 days. One patient who was treated initially with small amounts of BAL 13 hours after taking 10 Gm of mercury bichloride died on the ninth hospital day.

Nine patients took from 15 to 20 gm of mercury bichloride, 5 of the 9 having swallowed more than 15 Gm. Eight patients were treated with BAL from 1-1/4 to 3-1/2 hours after taking the mercury, 1 patient was first treated 19 hours after having swallowed at least 15 Gm. This patient was entirely well in 3 weeks, and the other 8 patients recovered completely in 2 1/2 to 7 days.

On admission the stomach was lavaged with 5 to 10 per cent sodium formaldehyde sulfoxylate, and 300 mg of a 10 per cent solution of BAL in benzyl benzoate and peanut oil was injected intramuscularly. One to 2 hours after this initial dose the patient was given 150 mg of BAL, which was usually followed in 4 to 6 hours by another dose of 150 mg. In several patients still a third dose of 150 mg was injected before 12 hours had elapsed.

Toxic reactions to BAL have taken the form of flushing of the face, abdominal pain, cardiac irregularities, sweating, shooting pains in the arms and legs and burning in the mouth and throat.

The evidence that we have been able to collect through the study of these 23 patients supports the contention that BAL is capable of neutralizing the toxic action of unusually large doses of mercury bichloride. The effects are most striking when BAL is administered intramuscularly in comparatively large amounts within 3-1/2 hours after ingestion of mercury bichloride. Under these circumstances the kidney appears to be spared serious or lasting injury, even when mercury can be detected in the urine for many hours after the ingestion of the mercury bichloride.

The outcome in any case of poisoning by bichloride of mercury is conditioned by many factors, some of which are quite beyond control, and it is therefore very difficult to estimate the value of one form of treatment, or a combination of methods, in a series of cases as small as this. The recognition of the loss of electrolytes and the danger of shock in the early stages, together with the introduction of the use of intravenous infusions of physiologic salt solution and glucose, reinforced by transfusions, when necessary, marked a distinct advance in therapy which has been employed in our patients. The introduction of gastric lavage with solutions of sodium formaldehyde sulfoxylate marked a still further step in advance, and though the value of this antidote has been questioned, we have availed ourselves also of its aid.

(Continued from page 204)

As a matter of fact, in the Indian School of Medicine, Madras, and presumably in similar schools, the students are taught the elements of modern medicine together with those of Ayurvedic or Unani system. Only, their knowledge of the former and often the latter is so poor that they are forced to practise a double quackery. In medicine, more than in other matters, little knowledge is a dangerous thing. However difficult and unpopular it may be, our political leaders must summon courage to decide that India will not be content with medievalism in medicine any more than in any other field.

SANTHANAM M.C.A.

THE CHOPRA COMMITTEE*

The Government of India have appointed a committee under Sir R N Chopra, I.M.S., to make recommendations regarding indigenous systems of medicine

The functions of the Committee to be fourfold, namely (1) the provision that should be made for research in and the application of scientific methods for the investigation of the indigenous systems of medicine, such as Ayurveda and Unani Tibbi, with reference to maintenance of health and the prevention and cure of disease, (2) the measure to be taken to improve facilities for training in Indian systems of medicine, (3) the desirability of State control of the practice of those systems of medicine, and (4) the other measures to be taken to increase the usefulness of the systems to the public as part of a comprehensive plan

Any institution which has served millions of human beings for a long time deserves respectful and sympathetic attention. The Ayurvedic, Unani Tibbi, Siddha and other systems have centuries of service and experience behind them. It is certainly necessary to conserve what is best in their drugs, dietetics and other methods of treatment. But it will be fatal to the progress of the country, if through mere reverence for the past, we seek a revival of ideas and practices which have been superseded, if not positively refuted, by modern scientific investigations.

One Science—Preventive and curative medicine is of such importance that it will be folly to surrender to traditional superstitions or beliefs. Ancient Indian astronomy and mathematics had respectable achievements to their credit. But if one were to propose that the Jantar Mantar should be renewed for making our astronomical calculations, one would be laughed at. To admit the superiority of modern mathematics or astronomical instruments does not in the least involve disrespect to our ancient mathematicians and astronomers. Similarly, to admit that modern anatomy, physiology and bacteriology, together with the mechanical, electrical and photographic appliances of wonderful precision constitute a scientific basis for medicine far in advance of the crude assumptions of our indigenous systems does not mean any disrespect to the latter. There cannot be two medical sciences any more than two mathematical or two physical sciences. In any field of human endeavour science has to be one and indivisible.

Both the layman and the practitioner of indigenous medicine will retort indignantly that many cases which have been abandoned as incurable by the Allopathic doctors have been cured by Ayurvedic or Unani treatment. That this is a fact need not be disputed. No one will claim that modern medical science has reached anywhere near perfection. It will be truer to say that the regions it has conquered constitute a very small portion of the fields it has yet to

* These remarks may also be useful to the 'Indian Systems of Medicine Committee, appointed by the Govt of Bombay under Dr J N Mehta

conquer All that is claimed is that its foundations have been scientifically laid and it is, therefore, capable of indefinite expansion Science is tested by its failures, and superstition flourishes by its occasional success While it may be true that many Ayurvedic and Unani drugs and methods of treatment have been found effective, the theory and reasoning behind them do not belong to the realm of science Their conclusions are not based on scientific measurement or chemical analysis and, therefore, there is little scope for methodical observation and research

Research — The only sphere for research in the indigenous system is regarding the effect of their drugs and dietetics Chemical analysis of the drugs and rigorous clinical observation regarding their effects may add a new and valuable chapter to modern medicine, but this research can be carried on only by persons who have been trained in modern scientific research and not by Vaid and Hakims who may be able to recite ancient texts, identify the herbs and chemicals referred to and prepare the drugs according to rule All that can be secured by research through Vaid and Hakims is to ensure that they conform strictly to the old prescriptions and prepare the drugs accurately and honestly It cannot lead them to discover why a particular drug produces a particular result and how it can be applied to other ailments

Health Statistics — There is another point which must be considered by all our provincial ministries who want to encourage the indigenous systems of medicine and thereby create many sets of practitioners who have no common phraseology, standards or measurements Public health legislation calls upon the doctors to notify to the health authorities infectious diseases How is this possible if in one area there is a modern doctor, in another a Vaid and in a third a Hakim? Similarly, how can the inspection of schools, factories and other places, where large numbers of people are gathered, be conducted unless there is a single standard for them all Our public health statistics will not be worth the paper on which they are recorded if they are not supplied in the same form and have the same degree of accuracy

Unfortunately the arrogant attitude of many Allopathic practitioners and their contempt towards the Ayurvedic and Unani physicians have produced a reaction in favour of the latter I am afraid this revivalist tendency is going to cost the country enormous wastage of effort and money The correct way of doing justice to the indigenous medicines is to assimilate whatever can stand the test of scientific observation and experiment with modern medicine A certain number of medical graduates should be specially trained in this field and attached to every big hospital They should be given special wards where they can experiment with Ayurvedic and Unani drugs and tabulate the results In the case of ailments not covered by these systems, the patients will be treated like others When any Ayurvedic or Unani drug has been found effective, it will be included among the Indian Pharmacopoeial list

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Original Contributions

TREATMENT OF TRAUMATIC SHOCK BY THE STERN METHOD

(INTRACISTERNAL INJECTION OF POTASSIUM PHOSPHATE)
AN EXPERIMENTAL AND CLINICAL STUDY

BY

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Of all the problems presented by the pathology of trauma there is probably none so complex, so imperfectly understood, and investigated so widely, intensively and from such diverse angles as that of traumatic shock, rather euphemistically called 'surgical' shock. The study of the growth of our knowledge regarding the phenomena of shock through the centuries is a fascinating subject by itself for it embraces the entire history of medicine. From the days of Hippocrates whose classic description of the clinical picture of shock cannot perhaps be bettered even to this date, practically every major advance of medicine has contributed in some measure towards the elucidation of this problem but the exact nature of the shock process still eludes us. To start with, its comparatively modern and unscientific appellation—"shock" (first attributed to James Latta, a Surgeon of Edinburgh—1771) is responsible to a large extent for the general air of confusion still surrounding this subject. In literature the word was (and still continues to be) used widely and loosely (e.g. shell shock, serum shock, toxic shock, gravity shock, etc.) and the scantiness of actual organic pathological findings in cases of clinical shock further confounded the issue. It was only with the growth of the modern concept of "Pathology of the Living" (a term originally coined by Sir John Bland Sutton) that the pieces in this great jigsaw puzzle started falling together to make a coherent whole. Hiatuses in this composite picture are still many and large, and it is in connection with one of these many doubtful pieces that I present this paper today.

Most of the modern work done to unravel and elucidate the shock phenomena have been concentrated on the humoral aspect of the problem. Rendle Short in 1913 first postulated that the essence of shock was a lowered circulatory blood volume—a theory that was

A paper read at the 68th Meeting of the G. S. Medical College and K. E. M. Hospital Staff Society, on March 8, 1947 with Dr. R. N. Cooper, M.S. (Lond.) F.R.C.S. (Eng.) in the chair.

established firmly and finally by the Shock Commission of 1914-18 under the joint control of Cannon and Bayliss. The circulatory volume loss was attributed to pooling in capillary areas and shunting of a large volume of blood from the general circulation. Again, it was at this time that the artificiality of division into primary and secondary phases was first realised and a serious attempt made to establish the universality of the mechanism of shock. The various earlier theories of nervous origin (Mitchell, Moorhouse, Keen and Crile) were relegated to temporary oblivion, or merely used to explain early manifestations ("Primary Stage") of shock. Further progress in experimental and clinical investigations localised the fluid loss by seepage of plasma in the traumatised tissue itself (Theory of local fluid loss—Blalock, Smith and others—1931). A new trauma hormone (apart from the H substance) was detected—(Moon 1938). The adrenal and the pituitary were implicated, biochemical changes in the shocked state—(eg increase of plasma potassium—Zwemer and Scudder—1940) were held to be of the greatest portent, and then as the pendulum swung back, the neurogenic theory was revived (O'Shanghnessy and Slome—1939). This time the more recently studied autonomic nervous system was held responsible and again a serious attempt made to collect, commandeer and adduce evidence in support of this theory, which attempted to explain the shock phenomena (or at least a fair part of it) on the basis of a gross depression of the sympathetic and overactivity of the parasympathetic nervous systems.

During the heyday of this period of shock research stimulated into feverish activity by the pressing needs of a total war—two articles appeared in the British Medical Press (*Lancet* and *British Medical Journal*), about the work of Lena Stern, Professor of Physiology, II Moscow Medical Institute, who claimed phenomenally beneficial results in shocked animals and patients by the introduction of Potassium ions into C.S.F. through Cisternal or Ventricular Puncture in order to stimulate directly the vegetative nervous centres of the autonomic system situated in the hypothalamus at the base of the brain. The work of Stern has excited some comment but little real interest in English or American Medicine as is evident by the extremely scant literature relating to it available in the *Anglo-American Journals*, and even some of these are contributed by Russian authors or translated from Soviet Journals. I am unable to account for this, unless it be attributed to a distrust of everything Russian, even though the USSR was then an ally against a common foe. For Stern, and her associates claimed very encouraging results of this treatment on war casualties on the Eastern front, even to the extent of eliminating the need for transfusion in cases of serious haemorrhage.

Briefly, the hypothesis on which Stern's work is based is this

Many experiments have proved that there exists an antagonism between the central and peripheral parts of the vegetative nervous system, as regards their reaction to the same substance—specially to the normal electrolytic chemical stimuli. This particularly applies to the ions of Ca and K. Changes in the concentration of these two

affect the activity of the nervous centres greatly—particularly any alteration of the co-efficient $\frac{K}{Ca}$. For example the Potassium ion has a very strong depressant action on the nervous system as well as on the heart when injected into the blood. This depressant action is mainly on the peripheral nervous system. But applied directly to the vegetative centres Potassium acts as a most potent stimulant. This paradoxical action of chemical ions is responsible for an automatic balancing of the effect produced by a substance injected into the blood stream, as the effect on the peripheral nervous system is to some extent neutralised by the passing of the substance into the C.S.F. and through it exerting a contrary influence on the centres. The presence of a selective haemato-encephalic barrier in C.S.F. formation naturally modifies to a great extent such neutralisation. While the direct application of Potassium to the nervous system has a stimulating action, any increase of the $\frac{K}{Ca}$ co-efficient has a similar effect and vice-versa. The calcium ion exerts an almost identically opposite physiological action—both centrally and peripherally. This physiologic behaviour of electrolytes in the C.S.F. was first demonstrated by Stern and Chvoles in 1933 by experimenting on normal dogs using a solution of KCl, and was confirmed by G. de Vleeschower working independently a year later. Acting on the presumption that traumatic shock is, in essence, a result of gross and widespread sympathetic paralysis with coincident parasympathetic hyperfunction, Stern and her co-workers first attempted to stimulate the sympathetic centres in shocked dogs by introducing Potassium ions directly into the ventricles. This produced an immediate, marked, and sustained pressor effect. The salt of potassium ultimately found by her to be the most effective was Potassium Phosphate and not Chloride as the Phosphate radicle further helped to raise the $\frac{K}{Ca}$ co-efficient by interfering with the ionization of Calcium present in the C.S.F. Further studies revealed that though in shock the plasma potassium is considerably raised and probably responsible for the marked degree of nervous depression, the concentration of Potassium in the C.S.F. was lower than normal with a consequent decrease in the $\frac{K}{Ca}$ co-efficient. Conversely, other workers (Vokressensky, Nodia) found that artificial alteration of $\frac{K}{Ca}$ ratio with a reduction of the co-efficient $\frac{K}{Ca}$ induced development of a shock-like state in experimental animals. Stern also found that injection of this solution intracisternally made with some force was quite sufficient for its entry into the ventricles and adequate for the purpose, haemorrhagic, histamine, peptone and traumatic shocks all were found to respond equally.

The scope of the present paper is limited mainly to the work carried out in this institution relating to the applications of Stern's method. Two groups of observations are presented. One, an experimental series on dogs and the other of clinical trial on patients suffering from traumatic and haemorrhagic shock. In all, 10 dogs and

10 patients were subjected to this treatment. Normally, I would have presented a small series like this with considerable trepidation and misgivings. However, I find from all available and accessible literature (many important references are in Russian) that most other articles deal with a similar or even smaller series of cases. In fact, there does not seem to be any reports of clinical trial of this form of therapy in Anglo-American journals at all, nor are many figures available. Even Lena Stern's figures are not published in her articles (translated from Russian) appearing in the *British Medical Journal* and the *Lancet*. I have hopes, therefore of being excused for the smallness of this series.

The solution used for these trials, both experimental and clinical, is the one recommended by Stern. Di and mono-hydrogen potassium phosphates are buffered together in a concentration of 1/6 gram molecular weight (Isotonic) and adjusted to a pH of 7.6 (Colorimetric)—this being the average normal pH of CSF. This optimal concentration of 1/6 molar potassium phosphate was arrived at by Stern after many attempts at trial and error, stronger concentrations are toxic—weaker strengths are not so effective. The solution was made in triple distilled water ampouled in 2 c.c. neutral glass ampoules and autoclaved. The usual bacteriological tests for sterility being carried out for each batch before either clinical or experimental use. The experiments were carried out on full grown healthy dogs (average weight about 9 Kgms) anaesthetised with ether administered through an intra-tracheal tube. In some, premedication with Amytal or Nembutal by mouth was employed. Atropine gr 1/100 was injected $\frac{1}{2}$ hour before anaesthesia in a few of the earlier experiments but discontinued later in order to prevent any interference with the autonomic nervous system. The blood pressure was directly recorded with a mercury manometer connected with a canula inserted in the carotid artery in the neck. The canula and connecting tubes were first filled with citrate solution. A floating indicator on the mercury in the manometer carried the writing lever against a slow moving recording drum. In this way some idea could also be obtained as regards the force and rhythm of the heart beat as well. The respirations were recorded indirectly by noting its depth rate, etc., at intervals. In every instance, only after all these preliminaries were arranged and a level blood pressure reading obtained was the shocking agent applied. The method of shock production varied. In the first four one or both lower extremities were crushed by hammering with a wooden mallet till the bone was fractured. In the next four the method was to bleed the dog from the femoral artery after exposing the vessel in the thigh. About 100 to 700 ccs (10 to 60 per cent of the blood volume assuming the total quantity of blood to be 1/7th of the body weight) of blood removal was necessary to produce the requisite degree of shock—the main guide to which was always the carotid pressure. The bleeding was not continuous or sudden—but stepped up in smaller amounts, 25-50 c.c. at a time, the whole process being spread over some time, about 10-15 minutes. In the last two the method employed was mesenteric traction. A loop of gut and its mesentery were taken out of the abdomen through

a small midline incision and continuous steady traction applied either manually or by tying it to a string with a weight attached

Cisternal puncture was carried out in most cases before the blood pressure had fallen to its lowest recorded level Potassium phosphate solution was not injected till the pressure had fallen to at least half of that originally recorded In one case it was repeated 4 times—a total of 5 cc The actual injection was made with force—with the dog's head in a lateral dependent position, in order that the solution should enter the ventricular system at once The results obtained in this series of ten experiments are summarised in Table 1

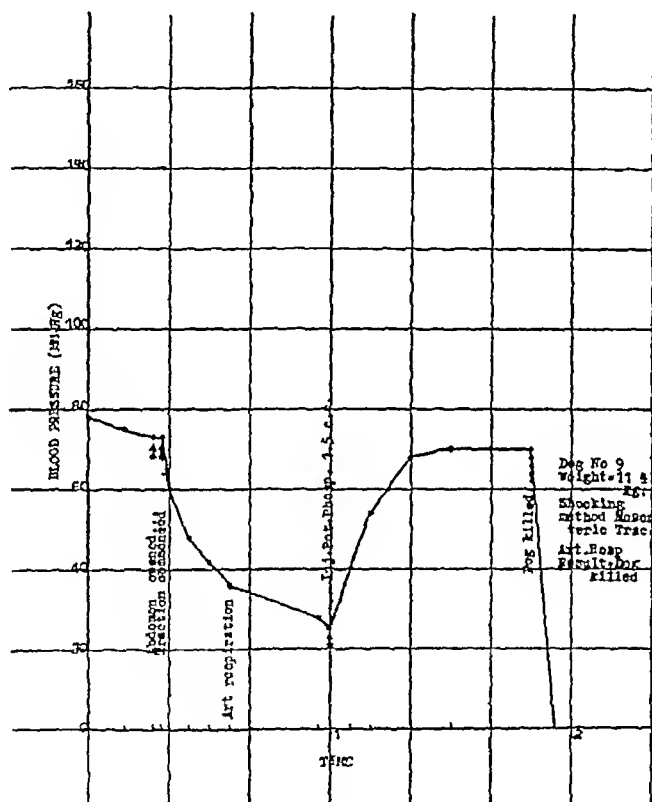


Fig 1—Showing changes in BP in dog No 9 during experimental shock and the effect of injection of Potassium phosphate Time in hours.

Smolik in 1943 published his results of similar experiments performed on 7 dogs The dose employed by him was much smaller 0.4 to 0.5 cc being considered adequate—on the basis of 2 cc for 70 to 75 Kilo man The weight of dog used by him varied between 15 to 18 Kilo Judging by his standards the optimal dosage for dogs in this series (7-12-Kilos) should be even smaller 0.03 to 0.04 cc or even less In this series however much larger doses were deliberately used—and only one death can possibly be directly attributed to this (Dog No 5) In fact considerable tolerance to larger doses was noticed Downman and McKenzie (1943) have also the same opinion

The immediate pressor effect produced by intra cisternal injection of K was found in every instance. The level and maintenance was however not constant. In six it was maintained for 15 minutes or more and in only three for more than half an hour. Response to second injections were very similar to that produced by the primary injection. The deaths of dogs 1 and 5 should in all fairness be attributed to faults in the technique rather than the injection, as the performance of a cisternal puncture on a dog is difficult on account of a very shallow cisterna magna and there was good evidence in these two cases of injury to the medulla produced by the needle. The heart rate and beat were invariably augmented soon after the injection and the respiration became deeper and somewhat quicker in most cases.

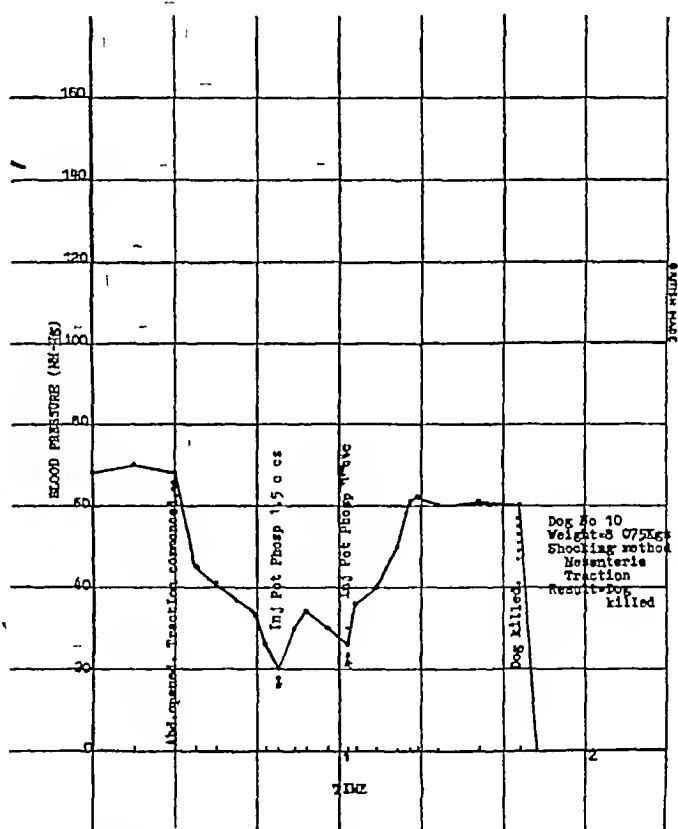


Fig 2—Showing changes in BP in dog No 10 during experimental shock and the effect of injection of Potassium phosphate. Time in hours

The conclusions of Smolik on experiments carried out on hypotensive dogs are some what different from those obtained from this series. He finds that while in normal dogs the pressor response of intra cisternal injection of K is definite and sustained, it is not uniform on hypotensive dogs. In this series the pressor response has been uniformly satisfactory though the same cannot be said of its

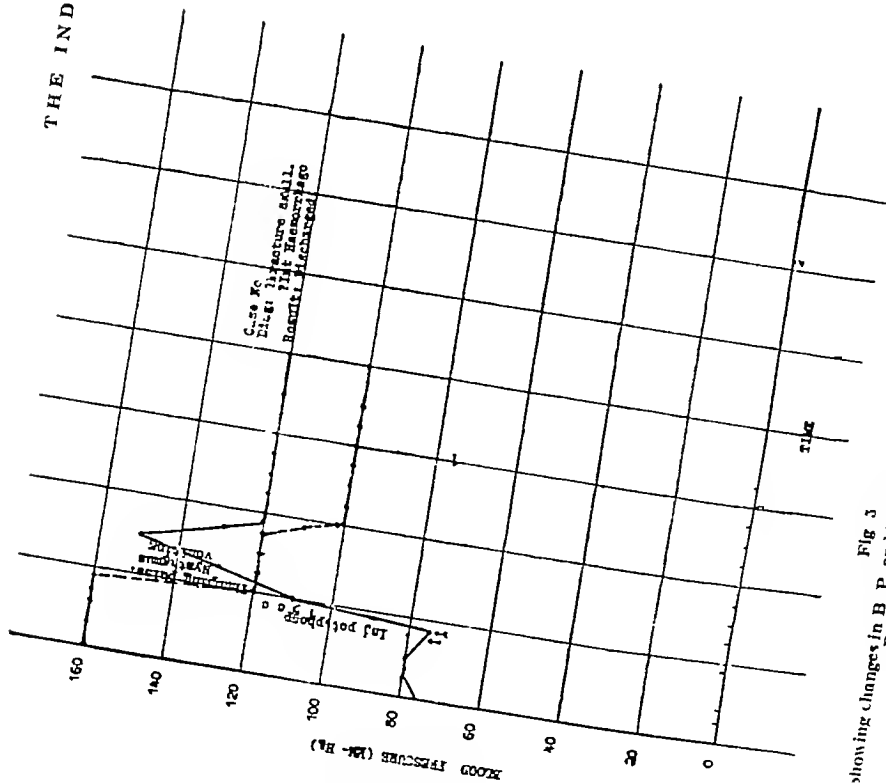


Fig. 3
Showing changes in B.P. and Pulse rate in Case 1 after injection of Potassium phosphate. Time in hours.

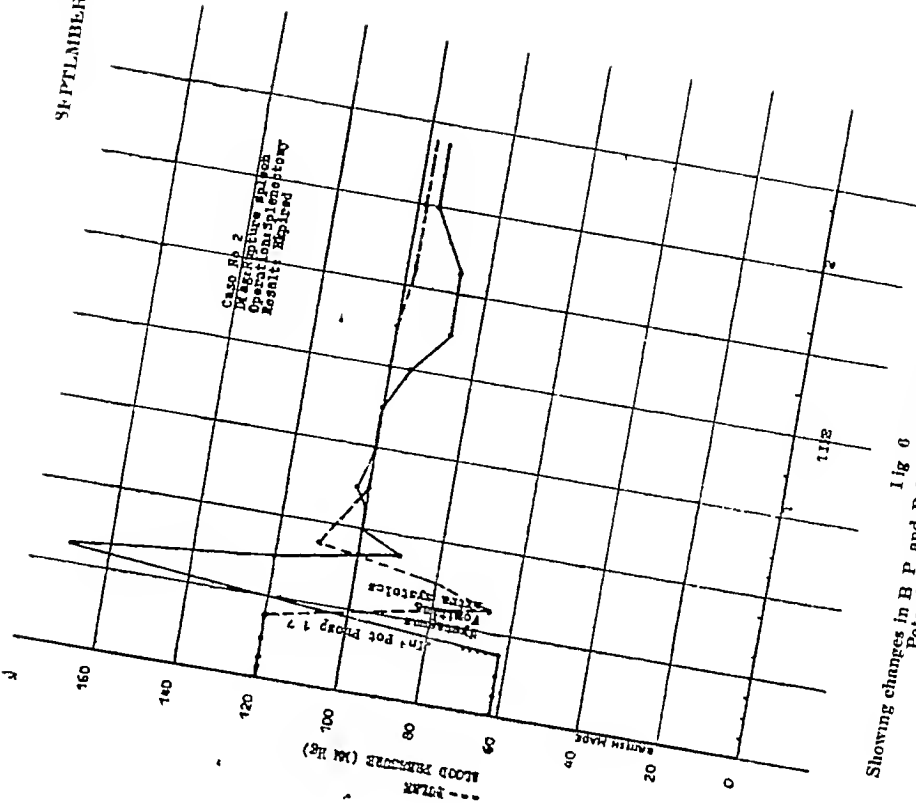


Fig. 6
Showing changes in B.P. and Pulse rate in Case 2 after injection of Potassium phosphate. Time in hours.

TABLE 1

CHART SHOWING THE RESULTS OF INTRACISTERNAL INJECTION OF P

No	Weight	Pre medication	Anaesthesia	Shocking method	Initial B P in mm of Hg	B.P. reached just before injection mm Hg	Maintenance time of lowest B P	Amount of K. Phos solution injected	Character and time of response	Time taken to rise to peak after injection	Level of peak mm Hg	Time taken to fall to subsequent level	Level of subsequent fall of B P mm Hg
1	11 Kg	Inj gr 1/100 atropine Sod Amytal gr 3	Intra tracheal ether	Crushing leg	70 75	25	5 Mts.	2 c c	Immediate 1 Mt	12 Mts	85 mm	13 Mts	80 mm
2	7 Kg	Inj atropine gr 1/100	do	do	60	5	1 Mt	1 5 c c	Immediate 2 Mts	15 Mts	45	4	25
3	9 Kg	Nil	do	do	75	15	1 Mt	1 5 c c	Immediate	9	55	12	35
4	9 75 K	Nil	do	do	60	40	1 Mt	1 5 c c	do	9	32	10	30
5	9 75 K	Nil	do	Bleeding 100 c c	64	25	1 5	1 5	do	9	35	4	45
6	9 75 K	Sod Amytal	do	Bleeding 100 c c	75	20	2 Mts	1 5	do	4	110	23	50
7	7 7K	Nembutal	do	Bleeding 300 c c	65	25 (fell to 10 once)	25	5 c c (Repen ted)	Slow at first Immediate after last Injection	10	70	10	68
8	10 15 K	do	do	Bleeding 150 c c	60	32	1 Mt	1 5 c c	Immediate	10	54	0	50 54
9	11 4 K	do	do	Mesentric Traction	78	25	1	1 5	do	28	70	0	70
10	8 075K	do	do	Mesentric Traction	68	20	1	1 5	do	30	62	5	60

were admitted during the riots or disturbances) quite often prevented a very thorough study. Nevertheless, as the results are encouraging even in this small series, they are presented here, if only to serve as a parallel for comparison with experimental observation. The ten cases which were thus treated for shock are tabulated below. It will

be seen that they were all adults or near-adults. The cases were chosen at random—no specific indication for this therapy being yet available—the only guide being the severity of shock as gauged by the systolic blood pressure and general clinical appearances. It is only fair, I think, to also mention at this stage that most of these earlier clinical trials were carried out on patients who were almost moribund, suffering from extreme shock, irrecoverable injuries or haemorrhages or very extensive burns, and as such one should not be unnecessarily prejudiced by the ultimate fate of most of these cases. The immediate results as may be noted are more satisfactory.

The most important and definite fact that emerges from a study of this series (Table 2) is that there was a response in all cases, may be transitory in some, but definite. It is also to be noted that in those three cases where the pressor response was short lived, the degree of shock was very great and chances of ultimate recovery practically nil. Errors of technique may also account for this. At any event, in the other seven immediate recovery from the shocked state certainly took place though in two cases it was partial and required additional routine antishock treatment, e.g. intravenous fluids, plasma, etc. In these seven cases subsequent intravenous fluids, blood or plasma were given at or following operation or later as required. There were no deaths which could possibly be attributed to the injection. Retching, or vomiting followed the injection in seven cases, but was transitory. Coarse, lateral nystagmus was observed in two cases for a few minutes. Apart from these and some restlessness which invariably followed the injection no other untoward symptoms were noted. In fact the procedure appears to be without any serious risks. The danger of injury to the medulla can be avoided by using a graduated thin flexible needle. It is probably easier to puncture the cistern than to do a lumbar puncture. The short period of restlessness which invariably follows the injection is often marked and very striking, and this sudden transformation of the quiet, apathetic state of the severely shocked patient into convulsive activity, with retching, vomiting, thumping pulse, augmented respiration, soaring blood pressure and a returning orientation is almost dramatic in some instances.

The only available account of clinical trials in shock appears in the reports of Stern's original work published in the *British Journals* (translated from original Russian). Unfortunately no figures or details are given. As far as I am aware no other reports of the clinical application of this method for shock have appeared in Anglo-American literature. The only report available of injection in human subjects are those of the work done by Ainslie and Dax (1944) on three psychotic patients. These patients were not shocked and were otherwise normal. Altogether eleven cisternal punctures were carried out on these patients at different times and Stern's solution was injected. It is interesting to note that they obtained a primary rise of blood pressure in only one case. This was also not maintained and even the respirations were not affected. All these patients had either normal or high pressures before injection. I have not tried injecting the solution in non-shocked patients, and so it is not possible for

me to explain this apparent discrepancy of behaviour. It is however quite possible that the response in a shocked individual is more definite, marked and sustained. In the normal individual with a normal blood pressure the various influences controlling and maintaining blood pressure are much more stable and much less likely to respond to or alter with extraneous stimulation than during the unstable equilibrium of a shocked state.

Naturally, as this trial was carried out only on shocked patients, controls were not possible, besides it would be very difficult if not impossible to get normal individuals as volunteers to study its physiologic action in man. But, in one of this series and in another case, normal physiological saline 1 to 2 ccs was injected with equal force before Potassium Phosphate was injected. There was a momentary improvement in volume and tension of the pulse, neither marked nor sustained. This was obviously due to mechanical stimulation of the centres by the fluid caused by the force of the injection.

It is not easy and hardly fair at this stage to assess the value of this new angle to the treatment of shock. Only extensive and controlled clinical trials can supply that answer. Besides, though the neurogenic aspect of shock has recently received so much attention, it must not be forgotten that the shock problem is far more complex and that this therapy cannot become a universal cure for shock. It is becoming increasingly clear, in the light of modern researches, that shock is a polygenic entity, and there are many types of shock according to the predominant causative factor. Even in a single case the genesis of shock is often multiple and various, and we deal with 'problems of shock rather than the shock problem'. Moon (1944) has attempted to analyse and separate these diverse mechanisms, a primary neurogenic, secondary toxæmic or 'capillary' origin, often complicated by a third the haemorrhagic factor. But to these we must add the various circulatory changes, e.g. peripheral vasoconstriction or dilatation, fluid imbalance, imbalance of tissue electrolytes renal dysfunction, and a host of other factors. It is possible, however, without much difficulty to sort out those cases which have a marked preponderance of neurogenic, or toxæmic or the haemorrhagic elements in them, and it will be readily understood that intra-cisternal injection of Potassium Phosphate is of the greatest benefit in the purely neurogenic types. But as it happens, the neurogenic factor operates more or less in all types of shock and even in those cases which are purely caused by haemorrhage, the neurogenic factor soon becomes a prominent feature. The peripheral vasoconstriction which follows is a protective phenomena caused by the overactive sympathetic and hyper-adrenalinaemia. If haemorrhage is continued the vasoconstriction gives place to vasodilation a state of sympathetic exhaustion. Theoretically it is in this stage of the genesis of shock that intra-cisternal is indicated. Stern, in fact warns us that the solution should not be injected during the first phase of sympathetic hyper-excitation. This second phase, marked by sympathetic paralysis corresponds with the so-called 'irreversible phase' of shock. Irreversibility of shock is a term that has been rather loosely used. It probably means that the vicious cycle of shock has progressed to a limit

beyond which the usual therapeutic measures, e.g., fluids, plasma etc fail to restore the circulating blood volume. In the earlier phases of shock with increased capillary permeability it is possible to check or even reverse the plasmorrhoea through the damaged capillaries. If allowed to continue this phase may pass into one with a state of decreased capillary permeability which makes reversal of the flow of tissue fluids impossible. Engel, in 1944, proposing sympathetic blocks in the treatment of traumatic shock, points out that these two phases of shock, namely the first, with increased permeability, and reversibility is produced by intense sympathetico-adrenal activity, and as the next phase develops with decrease in permeability and irreversible changes, signs of wide spread sympathetic paralysys become apparent. If Engel's assumption is correct, then in the clinical application of Stern's method we may have an answer to that phase of shock hitherto called irreversible. Engel himself advocates sympathetic blocks only during the first, reversible stage and intra cisternal potassium in the second, irreversible stage. Such an analysis certainly appears rational but awaits the acid tests of time and use. The experimental evidence is now quite strong but further clinical trials are necessary. Here a query may arise, How can a single injection of a small quantity of Potassium Phosphate in the cistern produce such wide spread and sustained effects in such a serious state as irreversible shock? An explanation in the light of the work of Stern and others may be hazarded thus. It is well known that the medullary and other automatic centres have a rhythmic activity. Alterations in the electrolytic balance, specially in the $\frac{K}{Ca}$ ratio is liable to effect changes in this rhythmicity. In the irreversible phase of shock, when the rhythmicity of the medullary centres is lost or markedly depressed, with attendant alterations in the $\frac{K}{Ca}$ ratio, it is quite conceivable that the introduction of an adequate amount of K by a single intra cisternal injection may restore the electrolyte balance and thus the rhythmic activity of the medullary centres. If the electrolyte balance is grossly upset, a further injection may be necessary to restore it. This raises another issue. In cases of very profound shock, should it be even better to carry out a slow perfusion of the hypothalamic and medullary centres with Potassium Phosphate solution through an indwelling cisternal needle? Such perfusion experiments have been done on animals through simultaneous cisternal and lumbar punctures, but have not, to my knowledge, yet been tried on human patients. It seems, however, to be worthy of a clinical trial in those very severely shocked patients in whom, intra cisternal injections of Potassium have produced only a temporary benefit—as happened in five cases in the present series.

Finally, it cannot be too strongly stressed that intracisternal injection of Potassium Phosphate does not in any way replace any of the accepted principles in the treatment of traumatic shock. Stern herself admits this. The real value of this treatment lies in its simplicity, and its probable benefit in the irreversible phase of shock. A moribund, shocked patient who is probably beyond even saline or plasma infusions may be so far improved with intracisternal potassium

as to respond favourably to the usual forms of treatment Two of the cases in my series fall in this category

Now I must record my thanks First they are due to Prof A S Poranjape who offered me every facility and gave me valuable suggestions for the experiments which were performed in the Pharmacology Laboratory of this College next to my past House Surgeons Drs Hanamant and Taher who assisted me with the experimental and clinical work to Professors Patwardhan Chitre, Amin and Monteiro who were responsible for making up the solutions from time to time for clinical and experimental use and to Dr Vaze my present House Surgeon for preparing the graphs I must also thank the Dean for permission to read this paper and my other surgical colleagues specially my ex chief Dr V H Kaikani for permission to use their cases for the clinical trials

DISCUSSION

Dr S B Gadgil enquired of the mode of action of Potassium Phosphate in the capillaries. He also wanted to know whether Potassium had a depressant action on the myocardium and also whether strychnine would be more useful than potassium in neurogenic shock

Dr J C Patel suggested to the speaker that the work should be extended in more cases of shock the cases being divided into three groups the first receiving only Potassium phosphate the second Pot phosphato and supportive measures like saline transfusions etc and the third as a control on conservative lines of treatment

Dr A V Baliga pointed out two features which he said may disturb clinician (1) restlessness and (2) a blood pressure which was even higher than the original obtained in these patients following injections of Potassium phosphate These features, he added, were detrimental one especially to in shock with internal haemorrhage He suggested that modification of the dosage might obviate this advantage

Dr R. N Cooper asked whether any ventricular punctures were done

Replying to Dr Gadgil Dr Sen said that the amount of Pot phosphate was too small either to have any effect on the capillaries or on the myocardium He added that strychnine acted mainly on the spinal cord and not specifically on the sympathetic centres Agreeing with Dr Baliga he said that a better selection of cases for this therapy was necessary He explained that during the early phase of shock when there was sympathetic hyperexcitation Pot Phosphate intracardially was contraindicated and in the two cases in the series that showed a rise of B P above the normal levels were probably in this stage He continued that this treatment should be reserved for cases in the paralytic stage of shock and that further investigation was needed to arrive at the proper criteria to judge the exact stage of shock

Answering Dr Cooper the speaker said that ventricular punctures were attempted in dogs but with poor results due to the difficulty in performing this operation

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TRENDS IN RECENT DRUGS AND DRUG ACTION

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The function of the pharmacologist is to explain the rational use of the new drug and possibly changes in the conception of action of old ones. E F Calkin has rightly said "Medical science is a developing tradition, neither a code of unalterable rules nor a formless collection of varying authenticity. Scientific spirit will tolerate neither a sterile immobility nor a rootless fickleness, scientific beliefs need periodic overhaul and constant adjustment"

So much of importance has been assigned to the new spectacular chemotherapeutic agents that progress in the treatment of systemic diseases has been neglected. It is proposed therefore to deal with these first.

Nervous System—Very roughly there are four main groups of drugs acting on the central nervous system, viz, the anaesthetics, the hypnotics, the analgesics and the drugs acting on the peripheral nerves i.e., the motor, sensory and the autonomic.

The anaesthetics—This year marks the centenary of general anaesthesia. Anaesthetics in surgery have evolved in four hops or stages. First there were the volatile liquid anaesthetics like Chloroform and Ether. Next the anaesthetic gases were in use and are popular even today in America. These include Nitrous oxide, Ethylene, Ethyl chloride and Cyclopropane. The gases were originally used for short operations but the technique for their use has been modified now for longer operations as well. The advantage of the gas anaesthetics is quicker induction with no bad after effects, though there is the risk of slight asphyxia with most of them. The next hop is the use of spinal anaesthesia, though correctly it is not to be designated a general anaesthesia as unconsciousness has to be induced by a basal narcotic. The disadvantage of spinal anaesthesia is the risk of respiratory muscle involvement or the diffusion of the drug upwards to affect the medullary centres. Fall in blood pressure has to be combated by prior administration of sympathomimetic drugs like Ephedrine. The last stage in the evolution of the general anaesthetics is the introduction of intravenous anaesthetics. These are of special interest to the practitioners who cannot have the services of a qualified anaesthetist. Hexobarbitonum (or Evipan), Pentobarbiturate (or Nembutal), and Thiopentone (or Pentothal) are the most popular intravenous general anaesthetics. (One gramme in 10 ml sterile distilled water run in at the rate of 2 ml per minute causes unconsciousness in 2 minutes). Spasm of the larynx has been noticed in some cases and this has been controlled by the injection of 5 mg of Tubocurarin, a drug acting at the motor nerve endings, reference to which will be made later.

The Hypnotics—The Barbiturates serve as a connecting link between the different groups of narcotic drugs acting on the CNS i.e., the anaesthetics, the hypnotics, the anti-convulsants etc. No less than sixty barbiturates are on the market, though only six are official in the British Pharmacopoeia. The basis for classification of the bar-

biturates is essential for the general practitioners, as several proprietary barbiturates appear frequently on the market. First, there are the stable barbiturates that are slow of detoxication and hence have a prolonged action, used mainly as sedatives in convulsions, epilepsy etc., e.g. Phenobarbitonum (or Luminal or Gardinal), Phemitonum (or Prominal or Mebaral). At the other extreme are the very unstable barbiturates that are quick in action and transient in effect e.g. the Hexo- and Thiobarbiturates which are used as general anaesthetics with a big dose of one to two grams, while the stable ones have a dose of 0.1-0.2 gram only. Between these come the intermediate ones which are popular as hypnotics with intermediate duration and dosage.

The duration of action of the less stable ones depends on the capacity of the liver to detoxicate, some drugs of this group being detoxicated in half an hour while others taking longer. Hence liver efficiency is very important in their action and use. To illustrate what is meant, if intravenous Hexobarbitonum is given to anaesthetise a man with an inefficient liver, he may never recover from the anaesthetic effects, as the liver is incapable of detoxifying it, with the result that the effect persists. The barbiturates are getting popular as suicidal or homicidal drugs. (The woman minister of education in the British cabinet is said to have died last month as a result of overdosage of one of the barbiturates). Picrotoxin 2-3 mg or sometimes even upto 7 mg every half an hour until seven injections, has been given with success in cases of barbiturate poisoning. (There is no fixed dose for picrotoxin. It is given until reflexes return, then repeated if reflexes disappear again and so on—Editor). Next to Picrotoxin, Leptazol (or Metrazol or Cardiazol) 100-300 mg (hypodermic or intravenous) is also found effective.

For convulsions and epilepsy, two substitutes for Phenobarbitonum are available today. (1) Phenytoin B.P.C. (or Dilantin sodium or diphenyl hydantoin, 0.1 to 0.2 g) is found effective. Di-ethyl-hydantoin (or Nirvanol) is found valuable in Chorea and post-encephalitic Parkinsonianism. (Hydantoin is a combination of urea with glycolic acid while Barbituric acid is a combination of urea with malonic acid). (2) Tridione 0.3 g has been found to be effective in petit mal and in psychomotor attacks.

The analgesics—One of the popular analgesics today is Pethidine (or Dolantin or Demorol). The interesting thing about this drug is that it combines in itself 70 per cent of the analgesic property of morphine and 80 per cent of the antispasmodic or spasmolytic property of atropine or papaverine. It is of great use in obstetrics in place of the twilight sleep. In doses of 25 to 200 mg it is found superior to morphine because of its wide margin of safety. It has no depressant action on the respiratory centre, no mental depression and does not cause constipation or urinary retention. It is available in tablets and ampules. Unfortunately it also a slightly habit-forming drug and even withdrawal symptoms have been noticed, though to a lesser extent than with morphine.

Drugs acting on peripheral nerves—Curare, the South American arrow poison, is finding a valuable place in medicine today, particu-

larly as an adjunct to general anaesthetics and before the electro-shock convulsions Curare prevents or blocks the acetyl-choline action in skeletal muscles. Though atropine antagonises the action of acetylcholine in the receptor organs in glands, heart and smooth muscles, no such action of it is in evidence in voluntary muscles, though it is noticed that in some cases rigidity in Parkinsonianism was controlled by atropine, through its central action. In animal experiments it was shown that Curarine, an alkaloid from Curare, leads to the formation of an impermeable precipitation membrane around end-plates and prevents the transfer of impulses to the effector cells. Curarine has therefore been found to be useful in relieving spasticity in hemiplegia, paraplegia, Little's disease, etc. But in anaesthesia, intravenous administration of 25 mg of curarine relieves the rigidity of muscles (There are several preparations of it on the market such as, Tubocurarine, Intocostin, Bulb-curarine etc.) Some anaesthetists in America use as much as 100-200 mg during a prolonged operation without any untoward effects. With the help of Curarine the anaesthetist can produce muscular relaxation without the dangers of deep anaesthesia. It is a drug to please the operating surgeon who keeps nagging at the anaesthetist! Myanesin, synthetic curare-substitute (B.D.H.) seems to be less toxic. When on the subject of adjunct to general anaesthesia one may mention another observation. Heart failure under general anaesthesia may be primary or secondary. Primary cardiac failure is probably due to ventricular fibrillation, or to cardiac arrest excited reflexly. When fibrillation is present, intracardiac injection of 5-10 ml of 2 per cent procaine may restore normal rhythm.

Circulatory Systems The Heart—Few practices in medicine have experienced so many swings of the pendulum as digitalis administration. In the past, many contraindications to the use of digitalis have been listed. Today one by one, these have been dropped out except perhaps acute infection like Diphtheria and Pneumonia. The present maxim is just the old maxim of William Withering "In the presence of a progressively failing heart, no matter what the cause, try Digitalis." A change in the conception of digitalis action on the heart has been effected by finding that it is the Aglycone or the non-sugar part of the Glycoside that is acting on the heart though the sugar part helps in the penetration and fixation of the active principle on the myocardium. To illustrate, Digitoxin is hydrolysed into Digitoxose, the sugar part and Digitoxigenin, the non-sugar part or aglycone. (The aglycone is chemically allied to the steroids of the bile acids, gonadal hormones, carcinogenic steroids etc.) The understanding of this fact will help one to realise the inconstant action of digitalis not infrequently noticed with different preparations. The hydrolysis is expected to take place on the heart where the sugar part helps the non-sugar part (or the aglycone or the Genin as it is frequently termed) to penetrate and settle on the myocardium. In many preparations, particularly the old ones or in some watery solutions, the hydrolysis has already taken place outside, with the result that the action is feeble or absent. Hence during the past ten years or more a new drug has been in use i.e. Digitalis lanata, a variety native to the Balkan States. This yields the active principle Digoxin or Digilanid.

C which is more stable Digoxin can be administered intravenously and acts in a very short time in doses of $\frac{1}{2}$ -1 mg The maximum effect is noticed in about 2 hours It can also be administered orally in 1-1½ mg doses, with a maintenance dose of 0.25 mg (It is also put on the market as Lanatosid-C or Digitaline-nativelle, Pandigal etc The confusing proprietary names are to be avoided and we must stick to Digoxin B.P obtained from the leaves of *Digitalis lanata*)

The old rule of William Withering still remains for the mode of digitalisation of a failing heart i.e., "Let the medicine be given until it acts either on the kidney, the stomach, the pulse or the bowel Let it be stopped at the first appearance of any of these effects" Lately *Digitalis* was observed to interfere with clotting of blood It may be of interest to know that two *digitalis* substitutes both from plants growing in India are being tested with very good results viz *Cerbera odollum* and *Oleander* leaves

Quinidine and its substitutes in auricular fibrillation—An interesting recent finding is that many substances other than Quinidine have the property of inhibiting auricular fibrillation Many of the local anaesthetics and spasmolytics have quinidinelike action The most promising of these is the Benzidine ester of piperidine ethanol called No. 25 which is 5 times as powerful as Quinidine Local anaesthetics like procaine spasmolytics like Syntropan, Trasentin and Pethidine,—all Atropine substitutes, have this action as well

Peripheral Vessels—Chemical studies of sympathomimetic drugs, i.e., adrenaline substitutes, have brought us quite a number of drugs of considerable value The reasons behind the quest for improved Adrenaline substitutes are the following Adrenaline has four distinct actions viz cardiac acceleration, vaso-constriction, bronchodilatation and cerebral stimulation All the four actions residing in the same drug is often a disadvantage For instance, if vaso-constriction is wanted as in vasomotor paresis, cardiac acceleration and bronchodilatation are unwanted side-actions With this object in view, chemists have been attempting to produce a pure vaso-constrictor etc Amphetamine (or Benzedrine) is one with dominant cerebral effects while Veritol (or Pholedrine or Paredrinol) is expected to be a pure vaso-constrictor Cobefrine and Propandrine are two other Epinephrine substitutes

A point of pharmacological interest about these vasoconstrictors is the fact that some of them are biphasic in action i.e., vasodilatation sometime follows the preliminary vasoconstriction The use of vasoconstrictors as nasal drops (Privine, Endrine, etc) in colds and nasal obstruction has revealed that indiscriminate and prolonged use of these lengthens the course of infection and often leads to sinus and ear complications

Vaso-dilators—For momentary effect, vaso-dilators like the nitrites are there, but real vaso-dilators for hyperpiesa are not available and perhaps are not wanted, as vasodilators don't form a line of attack in high blood pressure Potassium thiocyanate was proclaimed a few years ago to be an efficient reducer of blood pressure, but several delayed toxic effects have been noticed and the drug is advised to be given up

Capillaries — Capillary paralysis goes with Histamine action. Any substance with anti-histamine properties is bound to be of great value, in allergic and anaphylactic conditions. Benadryl is one such white powder, soluble in water and alcohol, active orally and parenterally. Benadryl neutralises the broncho constriction, vasodepression and spasm of smooth muscles caused by histamine. It is found to be of immense value in urticaria, angioneurotic oedema, and vasomotor rhinitis, of less value in asthma and still less spectacular in shock following burns. It is administered in doses of 50 mg four or five times a day. Drowsiness with dry mouth was noticed as side effect which may be prevented by 5 mg of Benzedrine sulfate.

Recently another anti-histamine drug has been put on the market as Imidazolin or Antistine. It is given in 0.1 gram doses intramuscular or even intravenous (slowly). It relieves itching remarkably, has no drowsiness as side-effects but in one or two cases there was momentary fainting.

The Alimentary system — Two conceptions of a revolutionary nature in the treatment of alimentary disorders have been brought to light. Firstly, purgatives as a class stand condemned today. Purgatives for constipation and purgatives for detoxicating are deemed irrational. There was a time when 3 grains of calomel twice a day for several days was the treatment of malaria, the malarial parasites were supposed to be washed out in the watery stools! Routine use of purgatives are to be condemned as the laxatives lose their effect and the bowels are weakened. Carefully selected diet is the most rational way of ensuring bowel action. Secondly, alimentary intoxication and therefore frequent use of the so-called intestinal disinfectants is yet another misconception that is correcting itself today. Frequent purgatives by keeping the bowels in a fluid condition enhance the chances of alimentary intoxication. More than this, saprophytic organisms in the gut are deemed friends and not enemies of man. Frequent and large dose of Sulphaguanidine revealed the fact that when the saprophytic organisms are killed, the host suffers from various vitamin deficiencies. In other words, the organisms of the gut synthesise vitamins or useful enzymes. It does not mean, however, that cholera and bacillary dysentery do not need gut disinfectants. Medical rather than surgical treatment is mainly indicated in Peptic ulcer. Several new gastric antacids are being tried and one need just mention that Aluminium hydroxide gel, Magnesium trisilicate and gastric mucin are popular today rather than the old alkaline carbonates.

Several of the new Atropine substitutes or derivatives have been found useful either as 'antacids' or gastric sedatives or antispasmodics. Flumydrine or Atropine methyl nitrate has been found useful in the treatment of congenital hypertrophic pyloric stenosis in 0.5 mg doses 4 or 5 times a day. Syntropan in 10 mg doses has been found to be a valuable antispasmodic of smooth muscle and Trasentin has a purely antispasmodic action. The work here is on the same lines as with Adrenaline substitutes i.e., to analyse Atropine actions and sort out the wanted and eliminate the unwanted actions by suitable chemical manipulations.

Liver—Toxic Hepatitis is said to be treated successfully by 3-8 gm daily doses of Methionine which is an amino-acid found in casein (Meat also contains both choline and methionine) Methionine has two actions, it prevents fat accumulation in the liver and also haemorrhagic necrosis. Fat accumulation predisposes to cirrhosis of the liver.

Choline orally in large doses of 6 gms daily for over six months produced disappearance of symptoms and signs of hepatic cirrhosis. The improvement probably was the result of lipotropic activity i.e., helping the liver to prevent fat loading and thereby a fatty liver. The actual fibrotic liver could not, however, be helped much.

Protein Hydrolysate—Recent work with the amino-acids has shown that not merely could glucose and saline be administered for basal conditions if the alimentary tract is closed for nutrition, but even amino-acids could be administered parenterally and maintain nutrition in starving individuals. In cases of starvation the nitrogen need may be more urgent than any other. In advanced cases of starvation, the gastrointestinal tract being below par, parenteral hydrolysed protein may alone save life. Chemists have evolved simple procedures for protein hydrolysis with papain and the hydrolysate is said to contain in addition to amino-acids some of the Vit B fractions. 5 per cent of protein hydrolysate with 5 per cent of glucose and 0.2 per cent sodium chloride, a litre of this twice a day may sustain life for a fairly prolonged period till the patient is capable of using the alimentary functions. The rate of administration of the hydrolysate is an important factor. Incidentally it may be mentioned that amino-acids have been reported to be of value in treating peptic ulcers and protein allergy particularly in children.

The Diuretics—Mercurial diuretics that have come to prominence lately are being experimented for improved application. A combination of Mersalyl with theophylline administered orally was found to act at least 80 per cent as effectively as parenteral administration. Gastro-intestinal irritation was not serious. One or two tablets t.i.d. for 2-4 days had no untoward effect.

Several reports of fatal results have been recently reported after intravenous administration of mercurial diuretics of the Injectio Mersalyl brand. They are therefore advised to be administered by the intramuscular route even in emergencies. Administration of plain ammonium chloride in congestive heart failure helped digitalis in many cases to exert a good diuretic effect. Ammonium chloride in addition to synergising mercurial diuretic seems to exert an independent effect.

Osmotic diuretics are also getting to be popular and of these Isotonic Sodium sulphate (42.35 gm in a litre) acted very well in emergencies. More than one litre can be given in uraemia due to renal inefficiency. Glucose 50 c.c. of 50 per cent solution also exerts a good diuretic effect.

After penicillin and the sulfa drugs, many of the former urinary antiseptics like Hexamine, Balsams, Dyes, Mandelic acid etc. have gone to the background.

Clinical Case Report

A CASE OF TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN, WITH CLINICAL RECOVERY

BY

N D PATEL, M D (Lond) M R C P (Lond)

Mrs P N aged 29 was in good health till October 1946 when she developed continuous fever which at first was thought to be enteric. After three weeks, signs of left pleural effusion were detected. At this time (Oct 21, 1946) the blood examination showed red blood cells 4.48 mil per c cm, 92 per cent haemoglobin, white blood cells 4,600 per c cm with 66 per cent polymorphs, 31 per cent lymphocytes and 3 per cent large nonocytes. The widal reaction was negative and the urine normal. The erythrocyte sedimentation rate was 34 mm at the end of one hour (Wintrobe). As clinical and laboratory findings were against typhoid fever, a diagnosis of tuberculous pleurisy was made. She had three children, two of whom were alive and well, but one boy aged 5, had died of tuberculous meningitis after 11 days' illness in 1942. On conservative line of treatment with rest, liberal diet, vitamins A and D, calcium and iron she improved, the temperature returning to normal and the weight going up from 83 lbs in October to 97 lbs in December, 1946. The X-ray examination on December 7, 1946 showed only a slight effusion at the left base, thickened left pleura and an irregular margin of the left dome of diaphragm. But the blood count had deteriorated a little, the red cells falling to 3.45 mil per cmm and the haemoglobin to 75 per cent.

She was advised to go to some hill-station for a change and while waiting at home in Ahmedabad before going to Abu, she developed pain in chest, fever, headache, vomiting, and nervous irritability in the second week of March, 1947. The headache was intense and daily got worse. It was associated with photophobia and insomnia. During the course of the next four or five days the vomiting became troublesome, and she developed marked neck rigidity and cranial nerve palsies,—left external squint, double vision, and left facial paresis. The physician in charge suspected development of tuberculous meningitis. I saw the patient on the 23rd March, 1947 in Ahmedabad and confirmed the physical signs of meningitis. The examination of the cerebrospinal fluid (see Table) removed the same evening (March 23, 1947) confirmed the clinical diagnosis of tuberculous meningitis. It was decided to treat her with streptomycin and she was put on a daily dose of 2 Gm of streptomycin intramuscularly (1 Gm dissolved in 8 cc of normal saline, and 2 cc injected every 3 hours) and 100 mg of streptomycin intrathecally on alternate days (0.80 cc of streptomycin solution diluted with 10 cc of normal saline injected slowly after removal of 20 cc or more of cerebrospinal fluid).

These injections were continued for 2 weeks. There were no toxic symptoms except a little erythematous rash and some vertigo.

Once when the dose of intrathecal streptomycin was increased to 125 mg she showed severe mental symptoms, such as restlessness, severe vertigo, diplopia and high temperature. During this period the temperature ranged between 100° and 104.6° and the pulse rate from 100 to 140 per minute, but the headache, vomiting and cranial nerve paresis had disappeared. Now the dose of intramuscular streptomycin was reduced to 1 Gm per day. After over a month of this treatment in Ahmedabad she was brought to Bombay on 29th April, 1947, where the treatment was continued till 23rd June, 1947, except that the intrathecal injections were made bi-weekly from 23rd May, 1947 till 19th June, 1947. On the 23rd June, 1947 all injections were stopped. The pathological changes in the cerebrospinal fluid during the course are given in the accompanying Table.

TABLE
Showing Changes in the Cerebro-spinal Fluid

Date	Turbidity	Cells	Lym phos	Polys	Protein	Glob lin	Sugar	Chlorides	Levin son test	Acid fast Bacilli
23 March 1947	SI turbid Cobweb++	210 per cmm	80%20%	0 3	+	—	750 mg per 100 c c			Nil
1 April 1947	SI turbid Cobweb++	207	85%15%	0 3	+	—	715			Nil
8 April 1947	, +++	250	85%15%	0 2	+	—	700			Nil
18 April 1947	, +++	105	80%20%	0 2	+	—	685			Nil
20 April 1947	, +++	92	85%15%	0 2	+	—	620			Nil
30, April 1947	Clear ++	68	Mostly Lymphos	0 2	+	+	600		+	Nil
6 May 1947	Clear ++	78		+	+	+	600		+	Nil
17 May 1947	Clear +	62		+	+	+	600		+	Nil
25 May 1947	Clear —	53	,,		+	+	600			
31 May 1947	Clear —	28	,,				600			
9, June 1947	Clear —	22	,,				600			
19, June 1947	Clear —	16	,,				600			

It shows the gradual fall of lymphocytes and general improvement in the condition of the fluid. The slight residual increase in the number of cells during the last month was probably due to the meningeal irritation by streptomycin. During the three months of treatment (23rd March, 1947 to 23rd June, 1947) the temperature ranged at first between 100° to 104.8°F and later 99° to 102.6°F, but the patient's general condition was so good that it was apparent that the temperature during the last three weeks or so was most probably due to streptomycin injections. The tachycardia which was persistent throughout was also to some extent the result of streptomycin injections, for both temperature and pulse rate returned to normal soon after stopping the injections of streptomycin and remained normal till the day of writing this report (August 15, 1947) i.e., for over eight weeks. The patient has no residual disability of any kind at present, is free from all symptoms and signs of meningeal irritation and her general condition is very good. The weight which had fallen to 87 lbs during the illness has now gone up to 112 lbs (August 15, 1947).

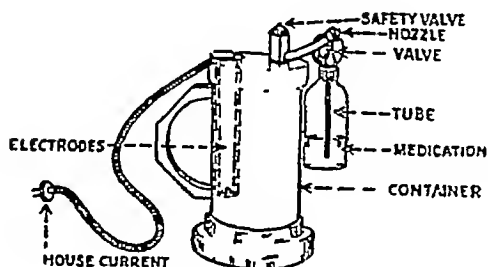
During the 90 days of treatment with streptomycin the patient had 105 Gm of streptomycin intramuscularly in 720 3-hourly injections and 3.2 gm of streptomycin intrathecally in 32 spinal injections.

tions She bore these injections very well, and except for the local discomfort of pain, and some skin rash and itching she had no untoward symptoms. Vertigo and cerebral irritability which appeared in the first fifteen days of treatment did not return again.

The diagnosis of tuberculous meningitis in this case was purely clinical, as no tubercular bacilli were shown in the cerebrospinal fluid and no culture or guinea pig inoculations were made, but the clinical evidence was clearly in favour of a haematogenous dissemination to the meninges from a tubercular focus in the pleura, which it was possible to control with complete clinical recovery by the prompt use of streptomycin in moderate dosage for a period of 90 days.

Critical Notes and Abstracts

A NEW AEROSOLIZER—Recent work on aerosols indicates that there will be an increasing demand for aerosolizers. Most models so far described have been too expensive for use on a large scale. Interest therefore attaches to a new simple model described by S J Prigal and F D Sper (Bulletin, New York Medical College, April-June, 1945, 8:21). This consists of a container which holds 16 ounces of water. Suspended from the lid into the water are electrodes, and five to ten minutes after switching on the current steam begins to emerge from the spout, which is so designed as to allow a thin trickle of steam to pass over a fine tube into the container holding the solution to be aerosolized. A safety valve in the lid allows the internal pressure to be varied from 8 to 50 lb. The rapid passage of the steam creates a vacuum in the tube, allowing aerosolized solution to be drawn up



and sprayed from the nozzle in a fine mist mixed with steam which can be safely inhaled six inches from the spout. A special screw valve controls the rate of flow, so that a given amount can be aerosolized in any given length of time. The 16 ounces of water are used up in

twenty to twenty-five minutes. The absence of water automatically shuts off the current.

Preliminary studies showed that with sulphadiazine (25 gm in 50 c cm water), blood levels of 15 to 12 mgm were attained in half an hour and maintained for four to six hours. In the case of penicillin, the findings in two patients treated with 180,000 units were that the blood level increased from 0.5 unit penicillin in half an hour to 2.12 units by the first hour, a level of 1.05 units being maintained for three hours subsequently. In the fifth and sixth hours there was still 0.128 unit per c cm of serum.

Book Reviews and Notices

OSLER'S PRINCIPLES AND PRACTICE OF MEDICINE 16th Edition revised by HENRY A. CHRISTIAN, 1947 D APPLETON CENTURY COMPANY, NEW YORK AND LONDON xliii + 1539 16 x 24 cm, 4 lbs price \$10.00

It is a pleasure to see this old classic in a new format, printed on good paper, and with an extensive index of 157 pages, in large type evidently meant for frequent use. The first edition of Osler appeared in 1892, and the first seven editions were carried through the press, by himself. In the eighth and ninth editions he had the editorial help of McCrae. It is the ninth edition (1920), whose final proofs were seen by Osler before his death in 1919, that this reviewer used as a text-book. The next three editions, 10th, 11th and 12th, were revised by McCrae alone. After McCrae's death in 1936, Henry Christian, Hersey professor of the theory and practice of physic (emeritus), Harvard University, and Physician-in-chief (emeritus) Peter Bent Brigham Hospital, Boston, has undertaken the editorial work, and has carried through the 13th, 14th, 15th and the present, 16th edition, which is revised and reset so much that it appears quite a new book. In the progressive and everchanging science and practice of medicine there have been innumerable changes and innovations during this period of over half a century, some fundamental some evanescent. James G. Carr of the North-Western University Medical School has written an interesting short history of medicine of this period, 1892 to 1947, as depicted in the 16 editions of Osler-McCrae-Christian. Perhaps there are still some physicians living who used the first edition of Osler as their medical text-book and who have kept themselves uptodate by reading the successive editions. Probably it will be rare to find a physician in the Anglo-American world who has not read Osler in some edition or other. As the publishers say, probably no other American text-book is as widely known and highly respected as Osler and in the 55 years of its publication they have seemingly distributed enough copies to supply a copy to every graduate of every American medical school with over fifty thousand copies left over for distribution to physicians in other English speaking countries, apart from many thousands of copies printed in foreign language editions, either authorised or pirated. We have compared this 16th edition with the 9th edition of 1920 on our desk and are pleased to note that all the good things of Osler, his diction, his apt phrases, his literary style, his historical references, are all well preserved here. The new additions and revisions made are thorough and uptodate. Christian is also a master of words and has a pleasing style of writing, clear and brief. There are many text-books of medicine in English, but in our opinion Osler-McCrae-Christian is still the best book to put in the hands of the medical student or the practitioner. The clinical descriptions in this volume have been based on personal observations of three masters of clinical medicine, and the new knowledge as it appeared periodically has been sifted and incorporated in the light of personal knowledge, experience and judgement. Many text books written by

multiple authorities are rather symposia, encyclopaedias or reference books, uneven in presentation and faulty in perspective

The changing outlook in modern medicine is well shown in this edition by Christian. Osler began his text-book with a masterly description of Typhoid Fever in 45 pages. Christian introduces medicine to his reader through the portals of Psychosomatic Medicine in 38 pages relegating bacterial diseases to a second place. Typhoid Fever which is becoming so scarce in civilized states is relegated to some 12th place, the first place in bacterial diseases being given to that "Captain of the Men of Death," Pneumonia (41 pages).

For long Osler was taunted as a therapeutic nihilist. The half century that has passed since the first appearance of Osler has been greatly fruitful in scientific therapeutic products and measures. These are incorporated in this edition with such meticulous care and discerning judgement that no one can call Christian a therapeutic nihilist. Christian has also introduced new terms for groups of infectious diseases and discussed them together in order to bring into closer correlation diseases apt to be regarded as entirely separate and distinctive entities, e.g. Salmonellosis, listeriosis, rickettsiosis, borreliosis, etc. We are glad to note that there is no section on Tropical diseases. We have always failed to see the justification for this section in medical text-books. The introduction of 'references,' citing chiefly recent papers, easily available, and older classics of the subject, is very welcome. The student is asked to read this section as an integral part of the discussion of a subject and we have no doubt that the student who avails of it will widen his horizon and be acquainted better with medical problems.

For the student or the practitioner who wishes to have a single Guru or Guide-in-general in clinical medicine, and who is desirous of inhibiting the 'culture' of scientific medicine as practised in Anglo-American countries, there is no better text-book than Osler-McCrae-Christian.

MARRIAGE HYGIENE a quarterly, second series edited by A.P. PILLAY with the help of an international editorial board published by the Editor, Whiteaway Building, Hornby Road, Bombay 1. Annual subscription, Rs 12 Sh 22, or \$5 50.

The first series of Marriage Hygiene which appeared from August, 1934 to August, 1937, had already established an international reputation, publishing articles on a variety of subjects such as sex, marriage, family, population, etc., when its publication had to be stopped because of financial difficulties. Its reappearance now, in times of paper shortage, labour difficulties, and social disturbances speaks well of its editor's courage and faith. We wish him luck and success. No one doubts the need for a journal dealing with problems of sex, or those arising out of marriage. We suggest the editor confines himself to these only, and, as Havelock Ellis desired, make this a journal of Sexology. With the list of eminent international editors and advisory editors, his task should become easy.

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Original Contributions

TRENDS IN RECENT DRUGS AND DRUG ACTION

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(Continued from page 225)

Salicylates in Rheumatic Fever —A rude shock has been given to medical men by some findings with reference to Salicylates in acute Rheumatic fever (1) The customary soda bicarb administration with soda salicylate is being questioned Addition of soda bicarb definitely retards the absorption of the salicylate Half the dose of the salicylate or even less without the soda bicarb is found to be more effective (2) Some findings even went to the extent of questioning the utility of salicylates in Rheumatic fever As gauged by erythrocyte sedimentation rate, salicylates did not influence in any way the course of the disease (3) High salicylate level in blood definitely showed toxic manifestations, particularly haemorrhagic diathesis like nose bleeding Many of the clinicians who had put down epistaxis, petichae or other haemorrhagic tendencies to rheumatic infections are being told to-day that the bleeding is due to the treatment and not to the disease Bleeding is more frequent after Aspirin (4) This bleeding could be avoided by concomitant administration of Vitamin K It has therefore been suggested that massive doses of soda salicylates should never be attempted unless vitamin K is administered simultaneously or even earlier (5) Gastric irritation by the salicylate is due to the release of salicylic acid by the hydrochloric acid of the stomach Soda bicarb is supposed to correct this But soda bicarb seems to interfere with salicylate absorption Hence enteric coated salicylates were administered Even here for some unknown reason gastric discomfort was still there Hence the adventurous American physicians are wantingly to administer salicylates by the intravenous route which is being stoutly opposed by the conservative British physicians

With these findings, salicylate therapy in acute Rheumatic fever is held in the balance General practitioners are expected to watch their cases on salicylate therapy and formulate their own conclusions

Haematology —One of the outstanding advances in haematology since the introduction of liver therapy is the demonstration of crystalline Folic acid which occurs in its conjugated form as a component of vitamin B complex It is effective in the treatment of Macrocytic anaemias with a megaloblastic bone marrow These anaemias include Addisonian pernicious anaemia, Sprue, Nutritional anaemia, Macrocytic anaemia of pregnancy and anaemia following total gastrectomy

When given in 10-20 mgm doses daily, it induces a prompt rise in the reticulocytes, a later increase in R B C and haemoglobin and all the recognised dramatic clinical manifestations of recovery under liver. The subsequent maintenance dose may be less. At present it can be said that this reparation is one of great promise which may completely supplant liver extract as a therapeutic agent especially in patients allergic to liver preparations. As understood today its mode of action is by accelerating the development of the immature red blood cells in the bone marrow and possibly influencing the metabolism of nucleic acid in these cells. Many green leaves contain Folic acid (the word Folic just means foliage or leaf).

Hodgkin's disease and Leukaemias —There is a very distant hope of curing or at best alleviating these fell condition. DEMA is a substance called also a Nitrogen mustard whose chemical name is Chlorethyl methlamine hydrochloride. The action of this substance is similar to that of X-rays or Gamma rays having a specific inhibitory effect on the growth of lymphoid tissue. More information is eagerly awaited.

Agranulocytosis —This is a condition due to sensitivity to a drug the more common causative agents being Amidopyrine, Sulpha-compounds, Gold preparations, Arsenic, Thiouracil etc. The condition develops only in a small percentage of cases receiving one or other of these drugs. Among the untreated, the mortality exceeds 50 per cent. After stopping the administration of the drug, administration of 40,000 units of Penicillin every 2 hours for a day or two promises to reduce mortality almost to nil. The mode of action of Penicillin, a chemotherapeutic agent in this condition of agranulocytosis is not clear to day.

Anticoagulents —Anticoagulents are being recommended for patients with coronary occlusion. At present, immediate administration of Dicumarol has been found to be effective, but it must be carefully watched. It causes a prolonged fall in prothrombin concentration lasting about a week or more. Orally 800 mg daily are given and in rare cases 5 mgm per kilo intravenously can be given. The action is evident in 24 to 48 hours. The dose is reduced to 50 to 100 mg daily when the morning prothrombin level falls to 50 per cent. This must not be allowed to fall below 35 per cent.

Endocrinology —The progress in Endocrinology during the last two decades has mainly been in the direction of the analysis of the glandular preparation, structural determination, attempts at synthesizing new analogue compounds etc.

Adrenal cortical hormone —Physiologically there is evidence that cortical hormone decreases capillary permeability. Cortical hormone also prevents wastage of sodium chloride and glucose from the system. In hypofunction of the adrenal cortex, there is depletion of sodium and chloride ions from the system, increase of potassium and wastage of glucose, the kidney fails to reabsorb the three. This action has given us the clue to treat Addison's disease by plain saline or administration of sea water. The capillary action has been utilised in preventing shock especially in extensive burns. The Calcutta School of Tropical Medicine advocates desoxycorticosterone, the most powerful of the three cortical extracts, in the treatment of Black water fever. Rationale is not quite clear.

Thyroid —Two of the recent advances in Thyroid therapy are (1) the use of goitrogens such as Thiouracil and propylthiouracil. The word goitrogens really meant reduction of activity of Thyroxine which probably had as its corollary, enlarged thyroid of a simple goitre type. Thiouracil and allied compounds act by preventing the utilisation of Iodine in the synthesis of Thyroxine. (2) The use of Radio active Iodine in hyperthyroidism. In hyperthyroidism orally administered radio active Iodine carried in about 1 mgm of ordinary Iodine gets concentrated in Thyroid and the beta rays from it act like roentgen radiation. Probably the same principle is involved in the use of "DEMA" in Hodgkin's disease.

Pituitary —The anterior lobe of the Pituitary with its multitudinous hormones still remains complex and its collaboration with gonadal hormones makes it still more confused. Most satisfactory results have been reported from the administration of Anterior Pituitary or the A P L Hormone from pregnancy urine in treating Migraine. It may also be mentioned that induced hypoglycaemia with Insulin gave relief to Migraine. Large doses of Nicotinic acid also relieves Migraine. These empirical treatments seem to indicate that the causation of Migraine is in the direction of carbohydrate metabolism error.

Gonadal hormones —These hormones remain as complex as ever. The synthesis of oestrogenic substances like Stilboesterol and Hexoesterol is a great advance. The oestrogens and the gonadotrophic hormones in general have revealed an important physiological fact that there is no specificity about the gonadal hormones, that they are biphasic in action *i.e.* oestrogens acting in man and androgens in woman physiologically. This apprehension is the basis for the use of stilboesterol in prostatic enlargement and testosterone in dysmenorrhoeas and certain lactational ailments. Recently some workers have noticed that stilboesterol has beneficent effect in tuberculosis, the hormone acting as a bactericidal agent. It has long been known that eunuchs have greater resistance to certain infections in particular to tuberculosis. Testosterone like stilboesterol has also a good effect in tuberculosis. Descent of the testes into the scrotum has been definitely hastened by male gonadotropins.

Vitamins —The achievements in the science of nutrition which has developed in recent years are among the most significant in modern science. The original five letters of the alphabet for vitamins have been extended and the original letters have been subdivided.

Vitamin K —A prolonged prothrombin time due to inadequate prothrombin concentration in blood is the chief characteristic of vitamin K deficiency. The deficiency is rarely due to vitamin lack in diet, but rather the inability to absorb the vitamin that occurs in a variety of foods. The vitamin works in collaboration with bile. The main indication are obstructive jaundice, haemorrhagic disease of the newborn, salicylate therapy, as a pre-operative precautionary measure etc. Haemophilia and thrombocytopenic purpura do not respond to this therapy. The B P addendum No 2 January 1941 has included Menaphthionum 5-10 mgm and acetomenaphthionum as vitamin K. The Americans call it Menadione. Natural sources for this vitamin are green leaves, cabbage, spinach, liver, vegetable oils etc.

Vitamin E —Chemically, vitamin E is alphatocopherol. Physiologically it is necessary for the healthy functioning of the testes and

developing embryo Healthy functioning of the nuclear chromatin seems to depend on vitamin E Although a good number of reports of the successful use of wheat germ oil and alpha tocopherol in sterility, habitual abortion, muscular dystrophies and amyotrophic lateral sclerosis have come, one cannot vouch for their utility In primary fibrosis, subcutaneous nodules, aching limbs or vague joint troubles, vitamin E seems to have done well Though styled antisterility vitamin, it does not enhance normal fertility Preparation Tocopherol acetate B P C 3-10 mgm

Vitamin D —In high doses of 200,000 units, vitamin D is said to have done well in several cases of arthritis and psoriasis Calciferol has also been used successfully in Lupus Erythematosus

Vitamin C —Vitamin C is said to decrease sensitivity to Arsphenamine when used in syphilis It is a valuable adjunct to liver therapy in exfoliative dermatitis

Allied to vitamin C is a new compound, not quite reached the status of a distinct entity called by some vitamin P This seems to aid vitamin C in preventing haemorrhage in experimental scurvy The active compound here is said to be related to Hesperidin and similar flavones and flavonal glycosides A methyl derivative of hesperidine is said to act by protecting against excessive capillary fragility which is frequent in arsenical haemorrhagic encephalitis Dietetic treatment of peptic ulcer seems to suggest the existence of a new vitamin U found in green grass stalks

Vitamin B —The complexity of vitamin B complex is not yet unravelled Thiamine (or Aneurine), Riboflavine and Nicotinic acid are fairly established Folic acid is now almost proved to be a part of the B complex Pyridoxin or vitamin B6 is known to have some effect in animals It has also been shown to have some effect in some forms of anxiety neurosis and vomiting of pregnancy in 25-50 mgm doses Similarly the W factor or Pantothenic acid, though having some effect in animals, its relation to human disease is not determined It may be of interest to some that Calcium pantothenate with para amino benzoic acid was administered to men and women with grey hair and it is reported that in several, the grey hair turned or tended to turn black Nicotinic acid 50 mgm I V is said to relieve Migraine The net result of the confusion in vitamin deficiencies is a healthy move to administer Multivitamins as it is difficult to diagnose threshold deficiencies

The second addendum to the B P published in 1940 is exclusively devoted to available vitamins

Chemotherapy —The year 1939 may be regarded as the beginning of the modern era in the prevention and cure of tropical diseases Increased communication with the tropics, particularly by air, was providing added stimulus to the control of tropical diseases undertaken for several reasons such as (1) war, (2) they were retarding commercial developments, and (3) possibly a lurking fear that they are being imported into relatively clean communities like America and Europe

Intelligent and intensive co-operation in experimental research between civilian and military groups in the United States and the British Commonwealth, not to speak of courageous clinical investigation on a scale previously inconceivable, made possible the rapid strides in the control of tropical diseases

Amoebicidal drugs —The position of amoebicides may be summarised “No antiamoebic drug thus far employed is infallible in sterilising an infected gut of *Entamoeba histolytica*, though there is evidence that each of them may contribute something to this end” Emetine still holds the field as the only drug to eradicate extra-intestinal amoebiasis In a high percentage of cases of dysentery, however, it is not curative The parasite tends to become resistant to the drug It is a drug with low therapeutic index or curative ratio as the toxic dose approaches the curative dose Single large doses and prolonged treatment are both bad Some controversy has been raised regarding toxic action of emetine on the heart The position could be summarised “If the recognised limits of dosage are not exceeded and if the patient is always kept in bed during emetine treatment, there seems to be little risk of toxic effects on the myocardium If it is forgotten that emetine is a potentially dangerous drug, in a careless treatment accidents may happen”

Carbarsone is a valuable alternative, better than acetarsol (or Stovarsol) A recent substitute to this is Carbarsone oxide which has been found to be superior exactly on the analogy of Mepharside over Arsenobenzols There was however a report of 0.25 gm b.d. for about 7 days causing death by haemorrhagic encephalitis and fatty degeneration of liver

Compounds of Iodine include Chiofior (or Yatren), Vioform (or Iodochloro hydroxy quinoline) and lately Diiodoquin These are claimed to be of use both in acute and chronic forms of intestinal amoebiasis Oral use has been supplemented by high retention enema A gram a day for two weeks showed no toxic effects The latest drug Diiodoquin, though with a higher iodine content than chiofior or vioform is absorbed from the bowel much more slowly Its action is slower so that 3 weeks instead of one week are required for a full course of treatment Cure rate is said to be in the neighbourhood of 95 per cent if coupled with emetine It has no contra-indications

Kurchi or the Indian amoebicide though established for its utility is not available for large scale use A Mexican plant *Chaparro amargoso* or *Castela Nicholsoni texana* has been found to be very useful and may replace Emetine

Britain swears by emetine, France by carbarsone and Germany by chiofior One presumes that we will swear by kurchi in course of time The standard treatment in the army is to have Emetine, Emetine Bismuth Iodide, Carbarsone and one of the Iodine compounds suitably spaced

Kala azaar therapy —95 per cent mortality has been converted into 95 per cent cure in Kala azaar by Antimony Neostibosan and Urea stibamine have become the antimony compounds of choice Total dose of 2-4 gms could be administered in a period of ten days, in 4 per cent strength in gradually increasing doses

Antimony is an easily excreted substance and so toxic or cumulative action is seldom experienced Unlike other chemotherapeutic agents, the effect is delayed i.e. the curative effect is perceptible only after about a week

In Sudan and occasionally in China, a kind of Kala azaar refractory to Antimony has been encountered For this, the aromatic Di particularly Stilbamidine was found very effective Che

compound is 4 Diamidino stilbene and is not an antimony compound 1 per cent solution beginning with 25 mgm and increasing to 85 milligram and so on daily for 10 days was found optimum The effect is seen after a week, the enlarged spleen goes down better here, than with antimony Children seem to stand the drug well It is also useful for Trypanosomiasis but not superior to Suramin (or Bayer 205) Diamidines can be toxic if administered incautiously Berberine an alkaloid from Hydrastis was found to be very effective in Oriental Sore and Dermal Leishmaniasis

Antimalarial drugs —Three eminent organisations viz, the National Malaria Committee of the U S A, the Malaria Committee of the League of Nations and the Military Medical Services have given their opinion on the best form of malaria therapy but they don't agree in all the details

Pharmacologically, alkali administration seems to aid quinine action and lessens the risks of toxic manifestations Quinine is more easily excreted than either Mepacrine or Pamaquine Pamaquin and mepacrine have no ecboic action while quinine has Regarding combination therapy, there is no advantage in combining quinine and mepacrine Simultaneous administration of pamaquine and mepacrine increases toxicity while quinine and pamaquine go well together The British army treatment for malaria favours the use of all the three *i e* quinine for the first two days, mepacrine from the 3rd to the 7th and pamaquine from the 10th to 14th day

Paludrine —Being a new drug, a more elaborate deal of the subject will not be out of place Paludrine hydrochloride is a colourless, slightly bitter drug with a solubility of 1 per cent The acetate is more soluble and is used for parenteral administration Paludrine is rapidly absorbed reaching a maximum concentration in 2 to 3 hours Subsequently there is a fall in the concentration but sufficient remains in the blood for about 12 hours The concentration in erythrocytes is about four times that in the plasma As much as 50 per cent is excreted in the urine and hardly a trace is left after a week of the last administration Its distribution in the body is similar to that of mepacrine

Unlike most other antimalarial drugs, it has been found to have an action on the so called exo-erythrocytic forms of the parasites This opens the subject of the growth of malarial parasites after infection in man An exo-erythrocytic phase in some deeper organ seems to be the cause for non-cure or relapse in man None of the older drugs seemed to have influenced this phase

Paludrine has been used successfully in the treatment of B T in relapse and delayed primary attack, and in M T in all conditions *i e* acute attacks, relapses etc With doses of 0.1 to 0.5 gm twice a day for about a week, acute attacks are arrested Subsequently 0.1 gm in one single dose once a week, has so far been found to keep the patient free from malarial fever Hamilton Fairly after an exhaustive study of this drug summarises as follows —“Paludrine is superior to all known antimalarial drugs in as much as it is a truer causal prophylactic in M T and a partial causal prophylactic in B T The only other drug that has a similar action is Pamaquine, but the drug has to be in dosage which is far too dangerous for routine use in man Paludrine in therapeutic doses controls malarial fever and terminates the attack. It produces a radical or permanent cure in the dangerous malignant type of malaria

The percentage of cure in B T is not yet known, but the Cairns results suggest that where individuals are not cured, the weekly administration of only one or two tablets would probably control relapses indefinitely until cure was obtained. Undoubtedly Paludrine is a triumph for British chemotherapy and is the greatest antimalarial drug known."

Paludrine then is the new British antimalarial drug. But how about the American cousins? "In the later stages of war, no less than 14,000 compounds were examined at a cost of about 2 million pounds. The work yielded considerable knowledge about the best way of using mepacrine and about the biology of the malarial parasites." The work also incidentally gave two new compounds of very great antimalarial value. This is not the place to go into the history of the discovery of the two compounds though it is very interesting. It just reveals yet once again that Germany is the source of most precious therapeutic agents. *Chloroquin* (or *Resochin* or S N 7618, *Santoquin* being its German precursor) has important advantages over mepacrine. Its absorption, distribution and excretion resembles mepacrine, but with this added advantage that it is colourless and does not stain the skin. *Chloroquin* completely suppresses M T infection and adequate treatment of clinical attacks produces a radical cure with the elimination of the parasites from the body. With B T the acute attacks are suppressed but relapses noticed if the drug is stopped. 0.25 gm in single dose once a week has the same effect as 0.1 gm of mepacrine daily.

Chloroquin then is deemed the American equivalent of paludrine and the Editor of the B M J in reviewing the drugs states that "*Chloroquin* has been tried on a much wider scale than has Paludrine but in many ways Paludrine seems to be the more promising of the two. American opinion on the other hand seems to be, "*Paludrine* has not as yet received as thorough clinical testing as *Chloroquin* but promises to be better than Mepacrine but not superior to *Chloroquin*." Arbitration, one thinks, should be left to neutrals.

But neither *Chloroquin* nor Paludrine can effect a radical cure in B T. Hence the quest for a new drug and this is supposed to be one at present going by the name of S N 13276 (S N 13276 has since been named Pentaquine *i.e.* 6-methoxy-5-isopropylaminoamylaminoquinoline). This is a pamaquin derivative and was really discovered when attempting to reduce the toxicity of pamaquin. Therapeutically S N 13276 is as active as pamaquin in bird malaria and is less than half as toxic as pamaquine to laboratory animals. Volunteers in an American prison infected with virulent strain of the south west Pacific strain of B T were treated with this compound (also with quinine during the acute stage) are declared to have been completely freed from the infection.

The British Medical Journal in its editorial on August 24, 1946 observed "The war had caused much suffering and destruction. It has however led to great improvements in our means of controlling and treating malaria. The scientific skill and capital invested in the war-time American programme of malaria research will yield dividend of improved health in the years to come."

Prevention of Malaria—One may be permitted before leaving the subject of malaria to refer to advances in the preventive line.

D D T or dichloro diphenyl-trichloro-ethane is one of the most powerful insecticides yet synthesised. It has put in the shade pyrethrum

the hitherto popular Dalmatian insect flower, lemon oil, Paris green etc. It is a white insoluble compound but soluble in many organic solvents. The dried powder is not absorbed through the skin, but the solution may. It is ordinarily used as a spray in kerosine solution (5 per cent usually). Insects like ants, mosquitos, flies, lice, bugs, cockroaches etc. when they come in contact with the solution are affected. The spot on which the solution is sprayed is said to keep away the insects for a fairly long time i.e. 10-15 days. Clothing impregnated with the solution of D D T is said to retain its insecticidal potency even after being laundered. D D T is said to have been a deciding factor in the winning of the last war.

Gammexene, also called 666, is $C_6H_6Cl_6$ is a substitute for D D T, is slightly more toxic but the effective dose against many insects is said to be 1/10 of D D T on the analogy of nupercaine to procaine.

Dimethyl phthalate, a colourless oily liquid when applied to the skin has been found to be an effective repellent of insects and particularly the vector of Kala azaar i.e. *Phlebotomus Argentipes*. Two others i.e. Indalone and Rutgers 612 are also being used as insecticides.

(When on this subject one may be permitted to mention that a powerful Raticide has been discovered in sodium fluoroacetate. It is superior to barium carbonate, thallium sulphate, arsenic trioxide and red squill.)

Antisyphilitic drugs —Arsenic and bismuth are complementary and not supplementary. Treatment with arsenic alone for 1-2 years did not prevent occurrence of nervous complications in 20-40 per cent of cases, while bismuth with arsenic from the very start reduced the occurrence very considerably. Bismuth when used as a negative ion seems to enter the blood i.e. as in Sobismanol or Iodobismatol orally.

The oldest arsenical, Arsphenamine or salvarsan of Ehrlich, still remains the most effective antisyphilitic drug. Mapharside is supposed to resemble the converted form inside the body after Neoarsphenamine administration. Mapharside is the drug of choice according to many, for the five day continuous treatment of syphilis. This is possible only in a hospitalised patient. Neohalarsan is a substitute for Mapharside. Both are said not to give rise to nitrotoxic reaction. The difference in the technique of administration of Mapharside group and the old Neoarsphenamine group is to be taken note of. Adrenaline is to be had ready for any eventuality when any arsenical is used intravenously.

Regarding the intramuscular arsenicals like Sulphostab and Thio-sarmin, the painlessness of the injection is sometimes its snare. This group of arsenicals is more toxic when administered intravenously.

The gradually increasing dose of arsenic as with antimony is not recommended by eminent syphilologists. Weekly or at most once in five days administration of arsenic 0.45 gm of the Arsphenamine group or 0.045 gm of the Mapharside group should satisfy the requirements. The duration of a course and the number of courses, not to speak of the intermittent, combined, or continuous alternate treatment, is left to individual clinicians. Pentavalent arsenicals like Tryparsamide and Atoxyl though more easily excreted can be more toxic, damaging particularly the optic nerve after some time of administration.

Bismuth —Usually oily suspensions are said to be better for exerting a prolonged steady action. Watery solutions are more irritant but more

easily absorbed and easily excreted. As substitutes for arsenic watery solutions of bismuth are sometimes given bi-weekly.

As for the treatment of syphilis with Penicillin the view seems to be gradually gaining ground (to quote Marshall) "No method of administration of Penicillin has so far in my opinion, surpassed the results obtained in early syphilis by the use of arsenic and bismuth in properly planned standard or rapid schedules. My own observations suggest that a treatment combining Penicillin with arsenicals give better results than Penicillin alone, and the risks are slight if the patients are carefully watched" (Marshall-Med Press-31st July 1946, p 77)

Sulpha drugs and Penicillin —In all the above subjects like anti-malarial, antidyenteric, antisyphilitic etc., the disease was the centre of the theme. When we turn to the Sulpha drugs and Penicillin, the drug becomes the centre of the theme. Chemotherapy of infections may be considered as synonymous with the pharmacology of Sulpha drugs and Penicillin.

The Sulphonamides —The medical public by now have acquired enough experience of the use of Sulpha compounds that any exhaustive deal of the subject is unwarranted. A pharmacologist would wish just to emphasise the basic facts governing their action. The organism causing the disease must be susceptible, though there is nothing to prevent experimenting in diseases with obscure etiology provided the condition does not need urgent attention with a more specific drug. Effective concentration should be maintained for optimum time in blood, c s f or surface. Inadequate therapy is still being encountered, though this is more the fault of the patient attempting self medication.

Pus inhibits Sulpha drug activity and it is here that Penicillin scores over it. Prolonged medication is to be avoided. In an acute condition, if there is no dramatic effect in 48-72 hours, the drug is to be suspended. Sulphadiazine and Sulphamerazine being more slowly excreted are the drugs of choice and the spacing of doses could be longer. Children and even infants stand the drug very well.

Recently it has been observed that it is possible to combine two or more different kinds of the Sulpha drugs in a single dose to get the combined effect of the different types. 37 per cent of Sulphathiazole, 27 per cent of Sulphadiazine and 26 per cent of Sulphamerazine formed a very good combination. Six grams a day of this combination had the same effect as 12 gms of other of these. (B M J Jan 4, 1947, p 7)

Penicillin —When we go from the sulpha drugs to Penicillin we go back from synthetic to natural products. But Penicillin can be and is being synthesised. In the beginning of 1946 a joint report of the American and British investigators gave the probable composition of Penicillin. Two formulae were presented that had only slight or subtle chemical variation in molecular arrangement. Recently Vigneud and Carpenter succeeded in synthesizing Penicillin. They coupled "Penicillamide, a compound related to the 'unnatural' isomer of the amino acid Cysteine with Oxazolone". It was proved conclusively that Penicillin was synthesized by the reaction. But in the near future there is no possibility of the synthetic substitute replacing completely the natural antibiotic.

In U S A four varieties of Penicillin are being recognised designated F, G, X and K. The last i.e. K has been found to be too labile for

therapeutic application The British and U S A methods of production from the culture seem to confer slightly varying properties Hence the need for a standard It is possible that the next edition of B P (for 1947) will have Injectio Penicillin oleosa containing 12,500,000 units of Calcium Penicillin, 4.5 gm of white bees wax in 100 c c of oleum arachis (dose 1-4 c c) One dose in 24 hours may suffice, as absorption and excretion are modified by the vehicle A few basic pharmacological facts about Penicillin should help in the rational use of this valuable therapeutic agent

Penicillin is an unstable acid but its salts are comparatively stable It is a readily absorbed drug when given parenterally Though orally it is not of therapeutic value, it is possible by adopting some technique to administer orally to be effective It is readily excreted and hence shows no cumulative toxic action It does not diffuse into C S F, pleura or serous membrane The value of Penicillin consists in its remarkable freedom from any side action on the tissue of the host it satisfies therefore one of the essential conditions for an ideal chemotherapeutic agent Chemotherapeutically it is a powerful antibacterial agent against gram positive organisms and certain gram negative cocci It is today claimed to be both a bactericidal and bacteriostatic agent unlike the sulpha drugs that are only bacteriostatic Organic matter, protein, tissue, pus or the tissue environment does not appreciably undermine its activity

Mode of administration —Buffered tablets are available for oral use Intravenous route is not indicated unless it is by the continuous drip method, as the drug is rapidly excreted Intramuscular route is the method of choice as the drug reaches the blood in optimum concentrations in about fifteen minutes The absorption may be slowed down to have a prolonged effect by suspension in wax and oil Otherwise the injection has to be repeated every four hours for the reason that it is quickly excreted For local application, continuous concentration has to be maintained The choice between powder, lotion, cream or paste depends on the condition partly and on the facilities available Sometimes for skin application, it is combined with Sulphathiazole or Sulphanilamide

Toxicity —Penicillin is remarkably free from toxic action, if the stuff is reliable After prolonged intravenous treatment a few cases of thrombophlebitis have been noticed Rarely generalised urticaria was noticed Fever, joint pains, cramps etc noticed with Penicillin therapy are traced to impurities As pointed out above, the method of extraction and manufacture, the British and the American methods being different, seems to confer slightly varying properties to different samples Benadryl 50-100 mg will control these allergic penicillin reactions

Use and dosage —The dosage is not quite established Roughly it may be said that subacute conditions need 200,000 units, acute conditions about 400,000 units and syphilis 3 to 4 million units, in the aggregate Individual dose and spacings are subject to wide range depending on the condition treated and the preparation employed Acute conditions demanding Penicillin are pneumonia, septicaemia, meningitis (intrathecally), subacute conditions like gonorrhoea and syphilis Skin conditions like sycosis and impetigo also respond well to local applications

Lately aerosol Penicillin, a fine suspension has been used as spray in respiratory infections. Besides its local action there was considerable evidence to show that it was absorbed from the mucous surface and the alveoli of the lung. Penicillin has also been used as chewing gum.

When considering the use of Penicillin it may not be out of place to refer to its abuse. It is estimated that about 70 per cent of the administered Penicillin today is an abuse rather than use. It is used in all vague fevers, in conditions of unknown etiology with dosage either too small or too interrupted or too prolonged. More often it is used as a prophylactic in the absence of evidence for its usefulness. This abuse is not fraught with serious consequences in the direction of morbidity, but more an economic wastage.

Other Antibiotics —1 *Patulin* from another Penicillin was being used in the local treatment of cold. 2 *Gramicidin* from soil organisms, Brevis, is used as surface bacteriostat, against gram positive organisms. 3 *Streptomycin* from soil actinomyces promises to be of great use against gram negative bacilli that are resistant to Penicillin and the sulpha drug. It is hailed as a drug of great value in tuberculosis. Parallel to this in the realm of Sulpha drugs are the Promin compounds —Promizole, Diasone, Marfanil etc. that are deemed to be of value in tuberculosis, leprosy, gas gangrene etc. but the early enthusiasm about these compounds is fast ebbing.

Chemotherapy and Drug fastness —This is an aspect of chemotherapy on which pharmacology laid special emphasis. Failure in chemotherapy is sometimes traced to the formation of a resistant strain of organisms. Ehrlich the father of chemotherapy had himself referred to arsenic resistant trypanosomes or spirochaeta.

Resistant strains in gonorrhoea have been noticed and they may be of three types: *i.e.* acquired, the relative and absolute. A resistant strain can be transmitted from one host to another, the strain retaining infectivity but refractory to the particular drug against which it has developed resistance. The development of the resistant strain is probably due to inadequate dosage, haphazard tests of cure, premature cessation of treatment by defaulters and last but by no means the least, self-medication. With sulpha drugs, self-medication is a menace. Inadequate dosage may produce an acquired clinical resistance to further drug therapy. The organism initially susceptible becomes desensitised to the further action of the drug either by being trained to rely on alternative metabolic process not affected by the drug as in the case of sulphanamides or by learning to synthesise an excess of metabolite capable of reversing the drug action. When such organisms may from an acquired case of gonorrhoea infect a fresh host, the resulting infections fail to respond to therapy and the organisms are further desensitised. Highly resistant strains thus develop and are passed from host to host, retaining the potentiality for mischief but refractory to treatment, thus causing a therapeutic problem.

Bacteriologists have noticed that an organism may become sulpha fast by continued cultivation in the presence of the drug. Once established, the drug tolerance may persist for long periods. This has been observed clinically as well. The nature of the modification has been of some academic interest. According to one theory of action of the sulpha drugs, the drug acts as a result of competition with the

bacteria for an essential. The bacteriostatic action is specifically neutralised by paminobed metabolite *i.e.* para amino benzoic acid. If the drug therefore acts by interfering with some metabolic process, it is not unreasonable to expect that sulpha fast strains might differ physiologically from the present strain *i.e.* metabolise by means of an alternative mechanism, not susceptible to such interference. Such physiological differences have been observed by bacteriologists who found that while sulphapyridine fast strains of pneumococci dehydrogenate glucose at a rate equal to the parent strain, they cannot dehydrogenate three carbon compounds like glycerol, lactate, pyruvate etc while the parent strain can. Others have also shown that sulpha resistance in *Staphylococci aureus* is associated with increased synthesis of paramino benzoic acid.

Fortunately the resistance is also specific and sulpha fast organisms are ordinarily susceptible to Penicillin and so on.

In America cases of infection in host population with Sulpha fast strains of pneumococci have been found and resistance to Sulpha therapy has been observed. As for *Gonococcus*, Carpenter and others have reported an increase in incidence of such strains from 15 per cent to 59 per cent in a period of 15 months in Britain and the Middle East.

It has been suggested therefore that this marked increase may be due either to development of sulpha fastness *in vivo* possibly through inadequate medication (in India I venture to suggest self-medication) or to an increased prevalence of Sulpha fast organisms arising as a consequence of the elimination of the susceptible strains by sulpha therapy. Time may reveal that this sad story is also true of Penicillin, though so far it has been claimed. Here is yet another strong case for the control of the sale of drugs.

A SIMPLE DEVICE FOR SPRAYING POWDERS

M K VAIDYA, M.B.B.S

and

V C SANGHANI, M.B.B.S, D.L.O

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A great need was felt in the Ear, Nose and Throat Department for some contrivance that could help the application of pulverised medicines with ease and certainty to the intricate and sensitive parts of these regions

Previously, there have been some attempts to get over this difficulty by a variety of insufflators none of which has stood the test of requirements for one reason or other. So much so that they were discarded and replaced by crude methods like gravitational instillation, paper cones, ear specula, and blowing by mouth or by Politzer's bag and various others which are all inefficient, unscientific, and sometimes grotesque.

The problem became particularly embarrassing when it was decided to try topical application of Sulphonamides to the raw tonsillar beds after tonsillectomy with a view to study their effects on sepsis, secondary haemorrhage, and period of convalescence. The fossae were deeply situated and vertical in position, the patient was unable to open the mouth sufficiently wide due to post-operative pain, and anything that carried powder to the fossae for contact application was unsatisfactory and painful.

Trying, therefore, to avoid these difficulties and find some instrument for the purpose, an idea was taken from Murphy's drip, and through a series of trials and modifications, a glass spray was evolved as something that was near best and cheapest.

The diagram (fig 1) illustrates the plain model and simple mechanism of its working in a clear way.

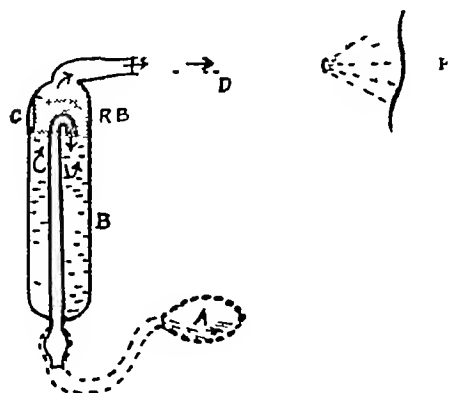


Fig 1—A—Bellows B—Powder in the spray C—the opening for filling powder covered by R.B.—a rubber band D—nozzle of required length → Directions of air flow with fine particles F—Tonsillar surface

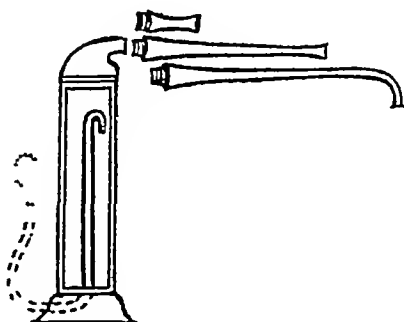


Fig 2—A metal spray, with extra nozzle for spraying the larynx

The powder is filled through the fenestration C which is then closed with a rubber band or with the thumb during use. Squeezing the bellows A with "adequate" force sends a controlled quantity of air through the tube which stirs up the powder and carries the desired quantity of its finer particles through the nozzle D to the confronting surface E forming a fine and uniform pellicle over it.

This instrument thus showed many outstanding advantages over all the previous methods which could be summed as follows.

(1) It is cheap and easy to work, (2) economises the drugs used, (3) never gets blocked or goes out of order, (4) sprays the drug aseptically & is untouched by hand, (5) throws only finer particles of powder, (6) thereby making a uniform pellicle over the surface, (7) application through a narrowly opened mouth becomes possible, (8) assures application in any plane and even in chinks and corners, (9) allows to control the force and quantity of application by the bore of the nozzle and force of pumping, and what is more, (10) renders the application entirely painless.

What came as a pleasant surprise and an important advantage during its routine use after tonsillectomies, was that because of the force and fineness of the particles shooting out of the nozzle, they got so well fixed over the raw areas of the tonsil beds, that unlike other dry or fluid surface applications, they were not easily displaced by the act of deglutition and thus a prolonged contact between the two was assured.

After this success, other applications for its special qualities were sought for. The nozzle was shortened and it was found useful in a large variety of other surgical conditions e.g. for the use of Boric, iodoform in perforations of the ear, for blind applications to the cavities left after radical mastoid, ulcers, burns, sinuses, toilet of recipient areas in skin grafting, and of operation wounds during suture and many other conditions where reliable, uniform, economic, aseptic, and what is still more important, atraumatic and painless application of powders is desired both by the surgeon and the patient.

A metal spray (Fig 2) could also be prepared on the same principle and though a little more expensive would be more lasting with an added advantage of being able to carry an extra nozzle for spraying the nasopharynx and the larynx, which is risky with a curved glass nozzle.

There may be many other uses it may be put to, and one may not be surprised if it finds a place on my lady's dressing table or among an artist painter's accessories. One thing is, however, certain that it will make a useful addition to a practitioner's room and to the general and especially the Ear, Nose and Throat Surgeon's instrumentarium.

Critical Notes and Abstracts

STANDARD TREATMENT OF EPILEPSY JERRY C PRICE, M D, New York, N Y and JOHN L OTTO, M D Galveston, Texas (Diseases of the Nervous System, November, 7 845-848)

Of epileptic cases adequately treated 50 per cent can be completely free of attacks, and additional 25 per cent are markedly improved and 25 per cent require special attention whether at work, at play or in school Thorough physical examination, neurologic survey, psychiatric investigation and laboratory study determines the socio-economic value of the epileptic person

Bromides, phenobarbital or a combination were the nucleus of the treatment of epilepsy The value of sedation was doubted The barbiturates seemed to have an "anti-convulsant," in contrast to the "sedative" effect It was found that two common elements had to be present in the structural formulae of the medicine that reduce the number of seizures The anticonvulsant property of a drug depends upon the relative concentration of these elements

The anticonvulsive property can be determined by passing an electric current through the brain of a test animal The amount of electric current required to cause the animal to convulse is tested and increased consistently by the medicines that are known to reduce the number of seizures and in doses that cause no toxic symptoms in the experimental animal The anticonvulsant effect of dilantin experimentally and clinically is greater than that of phenobarbital, bromides and other compounds structurally similar to it

An attempt is being made to standardize the drug therapy of epilepsy Fundamentally the drug acts in one of the two ways one is the drug depresses the function of nervous tissue, the second is the medicine, or some breakdown products, replace a chemical substance lacking in the epileptic and raising the convulsive threshold to or above its normal level

Unfortunately anticonvulsants have other properties causing unpleasant symptoms Sensitivity to medicines varies from person to person Successful treatment depends on the physician's ingenuity and experience to find the dosage of one or a combination of anticonvulsants suitable for the epileptic person

Standard treatment is that amount of medicine that will control the seizure with no unpleasant reactions The nucleus of treatment is dilantin, the initial dose of 0.1 Gm administered before bedtime The initial dose is small because toxic symptoms are commonly caused by starting medication with doses as large as 0.3 to 0.4 Gm The small dose is continued for one week, then 0.1 Gm is added each successive week until 0.4 to 0.5 Gm is being administered Increase is stopped in case of toxic symptoms in which case the dosage may be decreased by 0.1 Gm The medicine need not be discontinued completely to alleviate unpleasant symptoms, in fact, it is dangerous because status epilepticus may be induced Medicines should be changed slowly, for example, 1-3 months is required to change from 0.3 Gm of phenobarbital to a similar or larger dose of dilantin

Recurrence of seizures usually indicate inadequate dosages There are no tests to estimate the amount of dilantin absorbed and assimilated Overdosage symptoms are the only positive criteria to prevent inade-

quate therapy If after administration of the maximum dose the seizures recur phenobarbital is administered in increasing doses If the amount to control seizures also causes unpleasant symptoms, the medicines are unsuitable for treatment The alternative is to substitute mebaral for phenobarbital, continuing the maximum dosage of dilantin The same procedure for determining dosage levels is utilized with other medicines

If seizures recur after reasonable trial of the subtoxic dosage, dilantin is replaced by phenatoin which is administered similarly as dilantin Unpleasant symptoms caused by phenatoin are identical to dilantin except that it does not cause hypertrophic gingivitis Gingivitis is lessened during treatment with phenatoin even without massage and surgical removal of the excess tissue

This therapy is most effective in grand mal attacks, psychomotor seizures and psychic equivalents while petit mal attacks are affected least

8 to 16 Gm of glutamic acid daily reduces petit mal attacks in $\frac{1}{4}$ - $\frac{1}{3}$ of the cases

A new medicine is tridione, the first drug that reduced consistently the number of petit mal attacks The toxic symptoms are not too severe to enable to continue with the medicine and remain free of symptoms The unpleasant symptoms are visual, with larger doses drowsiness, lethargy and headache The dosage depends on the response of the patient and varies from 1-2 Gm a day given in divided doses of 0.3 Gm

Medicinal therapy is adequate only when administered alone or in combination in amounts large enough to control seizures without unpleasant symptoms Some cases do not respond to medicines, dietary surgical and psychiatric treatment are integrated to obtain best results

The only effective diet is the ketogenic or "high fat diet", it is most useful in petit mal seizures in children

There are cases that improve after surgical excision of a scar or "epileptogenic focus"

A mass of misinformation has accumulated in the public mind regarding causes and sequelae of epilepsy Psychiatric management includes thorough re-education of patient and relatives The patient is given instructions regarding medication, to return at intervals for readjustment of dosage until seizures are controlled The patient must be encouraged to understand and accept and live with his illness

In the epileptic child the responsibility for taking medication is turned over to him as soon as he is old enough Unnecessary restrictions should be removed Many epileptic children are more seriously handicapped by overprotective parents than by their seizures

Psychoneuroses and psychoses appear in epileptics in the same proportion as in the general population These illnesses respond to psychotherapy, insulin shock, electro shock or prefrontal lobotomy as well as in patients without epilepsy Epileptic equivalent states or post-seizure confusional states are often misinterpreted as behaviour disorders Mental retardation and toxic delirious reactions may be the result of toxic effects of anticonvulsive medication rather than deterioration Remarkable improvement is noted with proper medication and dosage

Book Reviews and Notices

CIBA SYMPOSIA a monthly journal, published by Ciba Pharmaceuticals Products, Inc., Lafayette Park, Summit, N J U S A gratis.

The daily post brings to most medical men a spate of leaflets circulars, blotting paper advertisements and even regular monthly journals from different drug manufacturing houses, praising their products, often running down their rival's. These literary efforts while attempting to educate the busy practitioner distort, suppress, or embellish scientific facts to suit their primary purpose of selling their own precious products. The House of Ciba is an exception to this, as far as the publication of a periodical is concerned. They are publishing a monthly, **CIBA SYMPOSIA** (in its eighth year of publication, which is free from any advertisement and self-praise. Each issue is devoted to some subject of cultural importance to physicians dealt with exhaustively from a historical point of view and illustrated profusely. We have received these numbers regularly since 1944 and cannot withhold our praise of the previous editor George Rosen, and the present editor Beate Caspari-Rosen, who have provided us with articles written by authorities on such diverse subjects as the History of Enema, the History of Salerno, the Doctor's Portrait, Artificial Mummification, Metabolism, Morphology, Medical Caricature, Clothing, Medical Geography, War Medicine, Apothecary Jars, Depth Psychology, History of Malaria, Bologna School, Fetish, Amulet and Talisman, Medicine in Utopia, Art of the Insane, Health Resorts, Health Museum, Ambulance, etc. We feel grateful to the editors and the publishers for their attempt to get the practitioner interested in the cultural aspects of his profession.

Announcement

The Registrar, Bombay Medical Council, announces that

(1) Medical Practitioners are reminded of the orders of the Government of India, viz., that yellow fever vaccine is available only at Government Institutions and they are therefore advised that it is improper for medical practitioners to give injections against yellow fever even though vaccine may be supplied by their patients, as it is very likely that such vaccine is either "not genuine" or "is such as has fallen into wrong hands" (2) It is notified for information of medical practitioners that the attention of this Council has been drawn to the inadequacy of after care arrangements at Temporary Surgical Camps organised by medical men and they are requested to note that any negligence in this respect will be taken serious notice of by this Council.

Honorary Secretaries, Fifth Bombay Medical Congress announce that the 5th Bombay Medical Congress will be held on the 15th & 16th November 1947 in Bombay. Members of the Medical Profession desirous of reading papers before the Congress should get in touch with the Jt Secretary, J J Hospital, Grant Road, Bombay.

Our Problems a forum for discussion

IMPOSSIBLE

"I can't believe that!" said Alice

"Can't you?" the White Queen said in a pitying tone "Try again, draw a long breath and shut your eyes"

Alice laughed "There's no use trying," she said, "one can't believe impossible things"

"I dare say you haven't had much practice," said the Queen "When I was your age, I always did it for half an hour a day Why, sometimes I've believed as many as six impossible things before breakfast" Lewis Carroll

Who would have thought possible the sudden Independence of India, the miraculous stoppage of carnage in Bengal, and the savage happenings in the unhappy land of the Punjab? How long does it take for a civilized man to revert to barbarism? We are living in an impossible world! Would some psychologist unravel the mysterious workings of the minds of our politicians Immense power has suddenly come to them what will they do with it? Destroy or build? Have they the requisite mental equipment?

"One of the characteristics of the new age is that you cannot take a step in any social or political scheme without involving yourself in highly technical and scientific questions It does not mean that scientists claim to be the Government or to have any other statutory position It only means that government and administration are impossible unless they are thoroughly scientific, in the sense of having people in control who know what they are doing We are very far from that position to-day But it is coming and it is one of the duties of the scientist to point out that this process must go on very rapidly if we are to escape in this country the position of being relegated to a relatively barbarian status" Dernal

Happily we have at the head of our government a unique thing in the government of nations—a Premier who is also a Minister for Scientific Development, and though by profession a politician, he is proud of his training in biology May he succeed in making possible things impossible and impossible things possible! No scientific-minded man is ever shy of 'miracles'!

THE LANGUAGE PROBLEM

Hindi will be the national language of India and in time all teaching institutions will adopt it as a medium of instruction There can be little doubt about that No nation can exist, can call her soul her own, talking in a foreign tongue But that does not mean that English language will disappear from schools and colleges At least for the next 30 or 40 years it will not be possible to teach modern science in *Hindi*, elementary science one may, but higher science no one can It must be obligatory for any student who desires to pursue a scientific career to take English as a second language from his school days Otherwise there is little chance for him following the modern scientific thought Teaching institutions which give up in a hurry English as a medium of instruction in science, will do it at the peril of total extinction from the world of science And what disaster will that be for India!

THE NURSING PROBLEM

A plea for remedying the scarcity of Nurses in the Province of Bombay
We read and find by our own experience that living costs are very

high and are still rising Food is up 250 per cent Clothing is unavailable without recourse to black market

Registered trained nurses are not sufficient for the need of the province They are agitating for more pay and reasonable hours of work limited to eight hours Anyone who knows the facts agrees that what they want is their just due But this increased pay of trained nurses with increased cost of milk, fruit and other foods is breaking the back of most of the charitable hospitals and treatment of patients in homes is becoming next to impossible

As regards private nursing homes, the charges for a bed per day have become beyond the limits of a middle class man and only the richest people can afford to have a private nurse at home Due to the scarcity of trained nurses, partially trained nurses and midwives have to be called in to attend a patient at a price ranging from Rs 20/- to Rs 25/- per day They seem to satisfy the doctors' wants with the limited knowledge they possess The American College of Surgeons finding a similar catastrophe have approved of creating a class of nursing attendants, nurse aids or the so called practical nurses for hospital duties with training limited from 6 months to a year

The evolution of registered trained nurses as a class in India has not been gradual as in England In England nurses used to get certificates after a course of two years in most of the hospitals in England and every hospital in London and provinces gave its own diploma to its nurses after training and examination in two years The nursing Council who laid down a standard of 3 or 4 years training was a later development

In India as in all countries a nursing course covering three calendar years after their matriculation turns many young women to other fields for careers for want of a sufficient dignity in society and there will always be a scarcity in this country if this course of three years after high school education is insisted upon as is the tendency at present in the different hospitals

When a patient is actually ill he must be cared for by a trained nurse but from observation and experience we cannot see why the ministrations of a trained nurse are necessary during the usual period of convalescence Surely any one possessed of fair intelligence and commonsense can wash and powder a patient, attend to his bed pan, carry the food trays, get drinking water and do the many little services that make for comfort and these duties plus some paper work make up the majority of working hours of most of the nurses

Women given short courses in practical nursing and then paid an adequate wage will fill a great need of the public in private practice and also hospital needs of many mofussil hospitals We request the Bombay Presidency Nursing Council to speed the day to put in operation such practical nurses and nursing aids

During the last war such trained nurse aids were produced with a three months' training Without such women who were attracted by good remuneration, nursing in hospitals might have been chaotic The fine work they did has proved that an intelligent person with a little training can assume a great part of the nursing needed in hospitals in private There are such unregistered persons who do general nursing in Bombay and command a wage of Rs 20/- to Rs 25/- per day before

they are available Even these nurses are very scanty and sometimes unavailable Why not officially create a class of such nurses aids so that they can be got in abundance in a country like ours for a more reasonable consideration by recommending a course of training of essential work to be finished in one year, and furnishing a certificate to that effect from the hospital authorities

S B GADGIL

Correspondence

Sir,

In present days, when the public is flooded with propaganda of reviving Indian "systems" of medicine, it had been refreshing to read the statement of B. T. Rao and of Santhanam in your esteemed paper (Febr. 47 p. 58 and Aug. 47, p. 203 respectively), as well as those of B. G. Vad and of Rai Bahadur Jaising P. Modi in "The Medical Bulletin" of 1-3-47 and 21-6-47 respectively

Western scientists also have to fight against the so-called systems, viz. Homocopathy, Naturopathy, Chiropractic, Christian Science, Back-to-Hippocrates-Movement, etc., which, by the way, are not fit to hold a candle to *Ayurveda*. I, therefore, hope not to appear as a presumptuous Westerner meddling in Indian affairs by submitting the following observations for consideration

INDIAN MEDICINE AND INDIAN MEDICINES

The present trend of "reviving" *Ayurveda* very often results in a disease being treated with indigenous drugs on the base of a "western" diagnosis. Doctors doing so are not practising Indian Medicine but merely dispense Indian medicines. A deplorable confusion is fostered by the advocates of *Ayurveda* between Indian Medicine and Indian Medicines. The latter are certainly welcome to modern science if and when their therapeutic efficacy could be assessed by modern investigations, and if the indications for their use are based on modern diagnostics. To call such practice, however, Indian Medicine is just as absurd as it would be if we talked about, say, Siberian Medicine because of some drugs which accidentally might have originated in Siberia.

The ways and means of proper *Ayurveda*, however, to arrive at a diagnosis and to prescribe medicines are fundamentally different from modern science as they are based on the doctrine of the "*Tridosha*". This doctrine is an outcome of the philosophic thought of antiquity (just as the doctrine of the 4 humours of the ancient Greeks) which, contrary to modern, empirical thought, subordinated experience to "*a priori*" laws sanctified by the authority of tradition. The *Tridosha* system, therefore, has its honoured place in the history of medicine, just as the humoral doctrine of the ancient Greeks is now a subject-matter rather for historians and philologists. Its practice (or malpractice) survived in India just as the bullock cart survived as a means of transport. But as the bullock cart is unsuitable for electrification, so the *Tridosha* system is unsuitable for revival by modern patching up, unless it repeats the scientific evolution of past centuries all over again. Such a course, however, would inevitably lead to a breaking away from the ancient, doctrinal thought until nothing would remain of it but its memory.

Panchgani,
Satara Dist.,
30-8-1947

K. EISENSTAEDT, M. D.

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KALA-AZAR OF UNDOUBTED INDIGENOUS ORIGIN DISCOVERED IN DRY AREAS

by
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and

N A PATKAR M B B S (Bom.)

(From The Department of Pathology, P G Singhane Hospital, BOMBAY)

Bombay and Poona have been recognised by specialists^{1,2} as regions outside epidemic and endemic zones mapped out for Leishmaniasis and termed by them as 'Dry Areas'. Yet we meet with cases here which turn out to be Kala-azar, both by clinical findings, biopsy and cultural evidence, but by a careful examination of their history they can be always traced to some endemic source and therefore are definitely 'Imported'. The case reported below, is that of one who contracted the disease in Bombay where he resided for some years before getting ill in January last. The only places he had been to, were villages in Poona Dist., where he was advised to go for a change as he was not showing improvement inspite of treatment, from where he returned in June last to Bombay, seeking admission into our hospital. The only justification for recording this case is that, it is the first case of Kala-azar contracted in Bombay proving the possibility of an indigenous case of local origin occurring in a 'Dry Area' for Kala-azar. It may be pardonable to give some details followed in dealing with a case of this nature coming to this hospital and the routine practice followed here especially when even a superficial clinical investigation in the Out-Patient Dept leads one to suspect Kala-azar.

Here are some details of the case and the methods employed in the investigation embracing mainly the following points —

(1) Name, (2) Age, (3) Occupation, (4) Residence, (5) History of the complaints, (6) Preliminary clinical findings leading upto the laboratory investigations of Blood including culture—a procedure which has been of value in confirming the clinical diagnosis and guiding specific treatment.

REPORT OF THE CASE

Name Ramchandra Balaji *Age* 22 years *Occupation* Petty salesman in a shop dealing in ladies' hand bags

Residence, and places visited (1) Avasari a village in Poona Dist. where he resided upto the age of 12 (2) Crawford Market area in Bombay where he has been staying for last 10 years except occasionally going to the above village for a change. During last 22 years of his life he did not visit any other place except Avasari Khed (village in Poona Dist.) and Bombay, all 'Dry Areas'.

History of the Complaint —

- (1) Pain in left hypochondriac region for last $1\frac{1}{2}$ months with a palpable swelling
- (2) General weakness for 2-3 months
- (3) Cough for 8 days
- (4) Pallor and wasting during last 6 months

On 25th December 1946 patient started getting intermittent fever (upto 101° - 102°). He stayed at home for 7-8 days and was admitted in to some private hospital on 4 Jan 1947 where he stayed for 22 days, during his stay in the hospital he was getting some type of Intermittent fever, he was discharged from the hospital and went to his native place (Avasari) in February 1947, where he stayed for about $1\frac{1}{2}$ months and returned to Bombay in April. As his general condition was not improving he went back to Avasari but again returned to Bombay in July last seeking admission into this hospital on 4-8-47

Clinical findings — Patient was emaciated, with yellowish tinge over the body, tongue, conjunctiva and nails were markedly pale. There were branding marks over left hypochondrium, Spleen was enlarged 7 ins below intercostal margin and 5 ins in breadth, the margin was sharp and firm to feel. Liver was not palpable, there was only Splenomegaly. Nothing abnormal was detected in Respiratory, Cardiovascular, Central Nervous, and Renal systems

Routine Laboratory Investigation —

From a finger prick, blood is collected aseptically in a pipette and distributed as follows —

- (1) Few drops in oxalate tube for Total R B C Haemoglobin percentage, and Total W B C Count
- (2) A drop in citrate saline for culture
- (3) On slides for smears for Diff. count etc
- (4) The rest is stored in the pipette for the serum to separate for Napier's Formol gel Reaction

Results —

- | | | |
|------------------------|---------------|----------------------|
| (1) Total R B C | 1 480 000/cmm | } Anæmia, Leucopenia |
| Haemoglobin percentage | 30.0% | |
| Total W B C | 2,000/cmm | |

- (2) Blood was stored in cold incubator (20°C) for 24 hrs and the deposit was cultured in Haemoglobin saline medium^s (Row), when examined after 9 days showed Leptomonous forms of Leishman donovani in abundance

- (3) Diff W B C count —

Neutrophils	75.0%
Eosinophils	00.0%
Basophils	00.0%
Lymphocytes	18.0%
Monocytes	7.0%
Premature cells	Nil
Parasites	Nil

- (4) Napier's Formol gel Reaction (Row's micro technique)* — Positive

Sternal Puncture Smear —

Positive for Leishman donovan bodies

Patient was discharged on 29-9-47 when following results were noted —

Weight increased by $2\frac{1}{2}$ lbs

Blood examination —

Total R B C	1,880,000/cmm
Haemoglobin percentage	50.0%
Total W B C	5,200/cmm

* A drop of serum is collected from the pipette on a clean glass slide and placed as a hanging drop over a watch glass containing 10 drops of commercial formaline so as to expose the drop to its vapour and was examined minute by minute. If the test is positive the drop shows signs of becoming milky white by the end of one minute and gel becomes complete by three minutes

Diff W B C count —	
Neutrophils	67 0%
Eosinophils	00 0%
Basophils	00 0%
Lymphocytes	30 0%
Monocytes	3 0%
Premature cells	Nil
Parasites	Not seen
Napier's Formol gel Reaction	Negative
Sternal puncture smear	No Leishman donovan bodies seen
Sternal puncture culture	No growth
Finger blood culture	Negative

Since writing this report, Heilig R & Raj Narayan Sachdev⁴ have also reported cases diagnosed as Kala-azar and occurring indigenously in Jaipur also a 'Dry Area' outside that mapped out for Kala-azar, but as this area is noted for Oriental Sore (*Leishmania Tropica*), there is just a possibility of the Kala-azar cases observed by these authors being generalised *Leishmania Tropica*, because experimentally *Leishmania Tropica* is capable of setting up generalised infection in susceptible animal like the white mouse⁵

In the light of Kala-azar being detected in 'Dry Area' one will have to revise the geographical distribution of this disease as mapped out at present

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Correspondence

Sir,

The city of Bombay will be the venue of many Medical and Surgical Conferences during the Christmas and New Year Holidays this year. It will be an unique opportunity for Bombay and Western India to search and collect materials and arrange an exhibition tracing the development of Medicine in India and particularly of Modern Medicine through the Portuguese and British periods.

I have been urging the organisers of Medical Conferences in India to arrange such Exhibitions as is done in connection with the Meetings of the British Medical Association. I was invited to give suggestions and even arrange for such an Exhibition at Travancore when the Science Congress was expected to be held there. But it was later decided to hold the Congress at Delhi. Lucknow Medical College has for some years arranged an annual Medical History Exhibition which I have always encouraged by suggestions and gifts.

I have just now before me, a report (See News & Notes) issued by the British Information Service, New Delhi, on a recent Exhibition in London, tracing the development of Surgery from Pre Historic times.

Will the organisers of the various Conferences confer and collaborate and make arrangements for a similar Exhibition at Bombay? I have no doubt that Western India has a great wealth of material to illustrate the History of Medicine Ancient, Medieval and Modern.

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AMOEBIC ABSCESS OF THE LIVER

by

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This paper is a statistical study comprising 180 cases of Amoebic Abscess of the Liver treated as inpatients at the K E M Hospital, Bombay, during a period of ten years from 1st January 1935 to 31st December 1944. A corresponding but brief study is also made of 66 cases diagnosed at the autopsy during the same period, out of which 12 are included in the 'clinical' series thus making a total of 184 studied cases.

Selection of cases Only those cases have been considered in which the condition of Amoebic Liver Abscess was confirmed at the operation or the autopsy table, or in which typical thick curdy yellow or chocolate coloured 'pus' was aspirated or was being discharged through the point where the abscess had burst externally. Doubtful cases as suggested by symptoms and clinical signs, fluoroscopic findings, moderate leucocytosis etc have not been included as they could not be differentiated from amoebic hepatitis—the stage preliminary to the abscess formation.

Incidence and Aetiology *Total incidence* The total number of inpatient admissions during the ten years have been 1,81,565. Of these the 180 liver abscess cases form 0.099 per cent i.e. approximately one case out of every 1000 cases admitted in the Hospital, turns out clinically to be a case of amoebic liver abscess. The post mortem diagnosed cases are not included together with the above as in many of them the finding of the liver abscess was incidental.

Table 1 Sex Incidence.

	Total No	and Percentage	Corrected Percentage
Males	127	97.7	94.1
Females	8	2.3	5.9

Sex incidence A marked preponderance of the disease in the male sex is evident. Out of the 180 cases, 127 or 97.7% occurred in the males, while only 8 cases or 2.3% occurred in the females. Even correcting for the low female attendance in the hospital as compared to that of the males, the average admission rate during the ten years being 28 per cent females to 72 per cent males, the proportion remains very much the same viz 94.1 per cent males to 5.9% females (Table 1). This is in accordance with the observations in various different parts of the world including those of Ochsner and DeBaakey (1943) who found 86.7 per cent of their 181 cases of amoebic liver abscess to be males. Preponderance of the males in having liver abscess is explained by their preponderance in the occurrence of intestinal amoebiasis, which is according to Manson Bahr 83.9 per cent. However why intestinal amoebiasis should have such a high incidence among the males has not yet been explained.

Age incidence In the present series no case has been met with in an infant or a child. This may be due to most of the children being

A paper read before the 70th Meeting of G. S. Med. College and K. E. M. Hospital Staff Society, on May 10, 1947, with Dr. P. Raghavan in the chair.

admitted at the neighbouring Children's Hospital. The occurrence of this disease is rare in children, but it has been observed even in infants, Niblock having reported a case in a Hindu boy aged 11 months and Des Barres in an infant aged 8 months. The minimum age in this series is 18 years, while the maximum is 62 years. The average age is 37 years, the maximum incidence being between the ages of 30 and 50 years, *viz* 74 per cent of the cases (as seen in Table 2).

Table 2 Age Incidence

Age Group	No. of cases	Percentage
Between 10 and 19 years	1	0.7
" 20 and 29	17	13.0
" 30 and 39	48	37.0
" 40 and 49	48	37.0
" 50 and 59	13	10.0
" 60 and 69	3	2.9

Yearly incidence. At the rate of 130 cases in ten years, the average yearly incidence turns out to be 13 cases per year. But this has not at all been constant year by year. Thus the maximum incidence is found in the year 1935, since when it is gradually but very irregularly diminishing. The minimum incidence is in the year 1940 (as seen in Table 3).

Table 3

Year	Total admissions	Amoebic abscess cases	Percentage
1935	11729	20	0.17
1936	12717	14	0.11
1937	12423	29	0.19
1938	13320	8	0.06
1939	11933	18	0.15
1940	12575	3	0.025
1941	13135	8	0.06
1942	12782	15	0.12
1943	14804	12	0.08
1944	16745	12	0.075

Communal incidence. Of the three principal communities seeking admission to this municipal hospital *viz* Hindus, Muslims and Christians, the Muslims show a comparatively much lower incidence (Table 4). In this series no cases were observed in the other communities but their members attending this hospital are too few.

Table 4 Communal Incidence

	Hindus	Christians	Muslims
Amoebic Liver abscess cases	98	20	12
Total admissions in 10 years	89,500	17,650	19,050
Percentage cases in own community	0.11 Per cent	0.12 Per cent	0.09 Per cent

The table shows that a large majority of the abscess cases—98 in the present series have been found among the Hindus but this is explained by the fact a majority of the population in the City and of those admitted into this hospital are Hindus. But the finding that the disease is twice as common among the Hindus and the Christians as among the Muslims is difficult to explain.

Occupational incidence. Most of the patients admitted to this hospital being from labour and poor class people, the majority of the cases in this series are naturally found to have occurred among them. Though in as much as the disease is almost directly proportional to

the insanitation, the better class people are bound to be less affected. No particular occupation appears to be aetiologicaly significant, the incidence among various occupations being fairly even.

Other aetiological factors (i) Previous attack of dysentery—52 cases i.e. 40 per cent of this series admitted, show that they had suffered previously from frequency of stools with blood and mucus. 18 cases i.e. 14 per cent positively denied ever having had such an attack. No mention regarding a previous attack of dysentery was obtainable in the remaining cases. This confirms the conclusion of numerous observers, notable among them being Craig, that amoebic liver abscess can occur in a person who may never have a full fledged attack of dysentery but may be suffering from a sub-clinical infection by the protozoon. (ii) The interval elapsing between the attack of dysentery and the liver complication—In 4 out of the 180 cases (i.e. 3 per cent) the dysenteric symptoms were co-existing with the liver abscess. In a large majority of the cases the interval was from 2 months to 5 years. According to the interval the liver abscess cases can be divided into two groups. (a) Acute onset—Arbitrarily those cases are included here in which the symptoms of liver involvement developed within 3 weeks after the attack of dysentery. Only 8 cases (i.e. 15 per cent) of the 52 who gave a positive history of dysentery, fall in this group. The shortest duration in this group is one day. (b) Chronic onset. Arbitrarily those cases are included here in which the symptoms developed after 3 weeks. Most of the cases viz. 85 per cent belong to this group. The longest duration in this group is 19 years. (iii) Previous attack of amoebic hepatitis. This has not been possible to record accurately and satisfactorily. (iv) Previous attacks of frequency of stools or of vague abdominal pains or discomforts without actual dysentery. This may point to the possibility of intestinal amoebiasis of long standing but such a detailed history was not elicited in most cases. (v) Chronic alcoholism. According to many observers chronic alcoholism plays an important part in the production of this disease by damaging the liver. In the present series of cases no positive history of alcoholism is recorded—perhaps not elicited. (vi) Climate. Hot, moist climates are thought to be the most favourable for transmission of this infection. Our climate in Bombay is thus very suitable especially just before and during the monsoon.

Table 5 Relative frequency of symptoms

Symptoms	No. of cases	Percentage
Pain in right hypochondrium	80	65
Swelling right hypochondrium	66	59
Fever continuous or in the evening only with or without rigor	55	42
Weakness and emaciation	16	12
Cough	15	11
Loss of appetite	5	4
Distension of abdomen	4	3
Discharge of purulent material through abdominal wall	3	2.3
Breathlessness	3	2.3
Vomiting	3	2.3

Symptoms The commonest symptom presented was pain in the right hypochondrium being present in 65 per cent of the cases. The most prominent symptoms were pain and swelling in the right hypochondrium and fever during some period of the illness (Table 5).

Other symptoms like pain in the right shoulder, yellowness of eyes persistent hiccup were each found in 2 cases while one case complained of pain and swelling in the epigastrium in the midline

Physical signs The most common sign elicited was tenderness in the right hypochondrium on palpation being present in as many as 124 out of the 130 cases (95 per cent). Next frequent finding was that of liver being both enlarged as well as tender in 108 cases (*i.e.* 83 per cent) thus in as many as 22 cases no clinical enlargement of the liver was detected

Table 6 Relative frequency of various physical signs

Physical signs	No. of cases	Percentage
Tenderness over the liver area	124	95
Liver both enlarged and tender	108	83
Fallor of tongue, nails and mucosae	76	58
Fine crepitations or friction sounds over the base of the right lung	26	20
Free fluid in the peritoneal cavity	5	4
Palpable spleen	7	5.4
Jaundice	1	0.8
Oedema over the liver area	1	0.8

Investigations followed in the present series

i Screening or Fluoroscopic examination—This was done only in 27 cases in all of which it showed the right side of the diaphragm to be raised and immobile while in one case it was mentioned that a circular dense area very suggestive of an abscess cavity could be seen in the liver substance

ii Examination of the faeces—Cysts of *E. histolytica* were found only in 3 cases—probably due to the faeces being examined quite a long time after they were passed

iii White blood cell count—This was done only in 83 out of the 130 cases. In 86 per cent of these cases the total count was above 10,000 per cmm. The differential count showed a varying degree of polymorphocytosis in a large majority of these cases

iv The abscess contents—These were obtained and examined in 118 cases. In 92 of these *i.e.* 78 per cent the 'pus' was described as typical chocolate coloured or anchovy sauce like. In the remaining 26 cases *i.e.* 22 per cent the pus was described as brownish yellow. In none of the cases where the aspirated material was subjected to bacteriological examination, was any growth of organisms obtained on culture, at the initial aspiration. In six of the cases, at subsequent aspirations growth was reported on culture the organisms being either staphylococcus aureus, *B. pyocyaneus* or *Streptococcus non-hemolyticus*. Trophozoite forms of *E. histolytica* were reported seen in the abscess contents of only two cases

v Sputum examination—This was done in 11 cases, mostly to exclude pulmonary tuberculosis. In none of these were *M. tuberculosis* detected while in one case liver cells were seen in the sputum the liver abscess having burst into the lung

It is felt that fluoroscopic examination and exploratory needle puncture if carried out in each and every suspected case would reveal many more abscess cases as distinct from hepatitis

Diagnosis Researches of Rogers and others have shown that in amoebiasis of liver prior to abscess formation there is a period in which

the liver is enlarged and tender—the stage of hepatitis. This may be acute—with high fever, marked leukocytosis and abscess formation in a few weeks—or chronic—with low fever moderate leukocytosis and abscess taking several months to develop. In either case the abscess may not develop. It is not only of great importance to diagnose amoebiasis of liver in this preliminary stage because prompt treatment would prevent abscess formation, but also essential to distinguish it from the condition in which a large abscess is present which may require drainage. This is often difficult but not if screening and inserting of an exploratory needle are resorted to.

Treatment Out of the 180 cases, 79 (*i.e.* 61 per cent) were admitted and treated on the medical side and 51 (*i.e.* 39 per cent) on the surgical side. The following were the two chief lines of treatment employed:

i One or more aspirations of the abscess contents combined with courses of emetine hydrochloride injections—75 cases were treated in this manner. 80 of these were aspirated more than once.

ii Incision and drainage combined with courses of emetine hydrochloride injections.

32 cases were treated in this manner. The approach in 27 of these was trans-thoracic with rib resection, while in the remaining five it was trans-abdominal due to the condition being diagnosed only during the exploratory laparotomy.

In the remaining cases all that could be done was an exploratory puncture or a few injections of emetine due to the patients dying in a few days after admission having come in a collapsed state or due to their leaving the hospital against medical advice. In all the cases the 'Emetine' injections consisted of either half or one grain of emetine hydrochloride dissolved in 1 c.c. sterile distilled water and injected subcutaneously once daily. Only in 8 cases was emetine hydrochloride (one grain) introduced directly into the abscess cavity dissolved in distilled water. Emetine is specific for amoebiasis of liver. Sometimes it alone has cured even large abscesses. But since Rogers in 1918 directed attention to the importance of treating this condition conservatively with combined use of aspiration and emetine that has been the treatment of choice. Craig believes that if the patients' condition warrants it, emetine alone should be given for a week and then aspiration or other surgical measures carried out as this markedly reduces the congestion and hence the chances of haemorrhage.

Result and mortality The following is the result irrespective of the treatment followed as shown in Table 7.

Table 7 Result and Mortality

	No. of cases	Percentage
Relieved	43	33
Cured	42	32
Expired	37	29
No change	8	6

Mortality in cases where the abscess perforated. In 14 cases the abscess perforated, 10 of which proved fatal giving a 71 per cent mortality.

Mortality and cured in relation to therapy. Out of the 32 cases treated by open operation (incision and drainage with 'emetine

injection) 9 (i.e. 28 per cent) expired, while of the 75 cases treated conservatively by closed drainage (aspiration one or more with emetine injection) 10 (i.e. 13.3 per cent) expired. In the above cases that were admitted in a low condition and died soon after operation have not been included in the open operation series, nor have cases been included in the closed drainage series where the patient expired soon after aspiration (Table 8).

Table 8 Mortality and cures in relation to therapy

	Closed drainage cases	Open drainage cases
Total	75	33
Expired	10 (13.3 per cent)	0 (28 per cent)
Cured or relieved	60 (80 per cent)	27 (72 per cent)
No change	5 (6.7 per cent)	

Incidence of relapse—Out of the 180 cases, 8 (i.e. 6 per cent) sought readmission after some time. Since a regular follow-up is not maintained in our hospital, the above cannot be said to be the complete figure. Relapse may be minimised if the intestinal infection which usually co-exists in a chronic form be separately treated by such amoebicides as emetine bismuth iodide or carbarsone.

The complications The liver abscess itself being a complication of intestinal amoebiasis, those arising in or due to the abscess are of the nature of further complications.

The most important complications have been 1. *Perforation of the abscess*. This has been the commonest and the most serious complication proving fatal in 71 per cent of the cases. The site of perforation has been varied.

- Perforation into adjacent viscera—There have been 3 cases all of which perforated into the right lung. Two of them had a spontaneous cure, the abscess contents being coughed out piece meal.
- Perforation into adjacent serous cavities—There have been 9 cases.
Peritoneal cavity—4 cases all proved fatal. Right pleural cavity—4 cases—3 proved fatal. Both peritoneal and right pleural cavities 1 case—proved fatal.
- Perforation through the skin of the abdominal wall—2 cases one expired.

As with other authors, the pleuro-pulmonary involvement is found to be the most frequent and this has been attributed to a majority of the abscesses developing on the upper surface of the right lobe.

Secondary infection of the abscess with pyogenic organisms

In six cases secondarily infecting organisms were grown on culture. This cannot be taken as the true figure as the aspirated material was not cultured every time and in some cases not even once.

Liver abscess cases detected at the autopsy During the ten years from 1st January 1935 to 31st December 1944, 3946 autopsies have been performed at the K. E. M. Hospital, out of which amoebic liver abscess was detected in 60, giving an incidence rate of 1.7 per

cent During the same period pyogenic abscess (*i.e.* cholangitic, pyelo-phlebitic and pyaemic—as distinct from tubercular or gummatous processes) in the liver was found only in 15 autopsies

Out of the 66 amoebic abscesses, in 15 the finding of the lesion was incidental in as much as the abscesses were very few and small or healed and the death was due to some severe lesion in other organs

Yearly incidence has varied greatly (as seen in Table 9) but it closely corresponds with the frequency with which amoebic ulcerations have been detected in the colon at autopsy

Table 9 Yearly incidence of Amoebic Liver Abscess and amoebic ulceration of colon-at Autopsy

Year	Total autopsies	Amoebic liver abscess [No Percentage	Amoebic ulceration colon No Percentage
1935	280	8	12
1936	414	0	30
1937	403	5	27
1938	582	17	53
1939	530	10	40
1940	303	1	16
1941	859	7	12
1942	340	2	0
1943	441	3	14
1944	200	5	0

It is interesting to note that in the year 1940, the incidence of all the three groups *viz* 'clinical' abscess cases, 'autopsy' abscess cases and 'autopsy' ulcer cases markedly diminished after reaching a peak in the year 1939. The low incidence among 'autopsy' abscess and ulcer cases is kept up but a gradual increase in the number is noted among the 'clinical' cases in the following years

Sex incidence Of the 66 cases only one was female while the rest 65 were adult males. Here again the marked preponderance among the males is well brought out. In Gharpure and Saldanha's series of 169 autopsy cases analysed in 1931, 97 per cent were males.

Number and site of the abscesses in the liver In 22 out of the 66 cases there were found more than three *i.e.* multiple abscesses. Two abscesses were seen in 9 cases while three abscesses were met with in only one case. In the remaining 34 cases (52 per cent) there was a solitary abscess. The largest size recorded was 18 cms diameter, while 4 of the solitary abscesses were quite small being less than 1 cm in diameter, but confirmed to be amoebic in origin histologically.

Table 10 The abscess contents

	No of cases
Thick curdy yellow with admixture of white or red	35
Thick and greenish	0
Nil—the abscess being healed	14
Not described—the abscess having totally burst	8

The commonest site was right lobe and particularly its superior surface for the solitary abscess. Both the lobes were affected in 20 cases.

The abscess contents In most cases the contents were described as necrotic, the usual colour being yellow with admixture of white or red while the usual consistency was thick and curdy (Table 10).

The so called typical chocolate or anchovy sauce like 'pus' is held to occur only if hæmorrhage has taken place into the abscess.

cavity, or where liver tissue is being extensively destroyed, or where the abscess has burst into and intermingled with the lung parenchyma

Concurrent presence of amoebic ulcers in the large intestine

Out of the 66 there were present in 51 cases amoebic ulcers distributed in the various anatomical divisions of the large intestines as shown in Table 11. But in the remaining 15 cases (23.5 per cent) no ulceration was detected in any part of the large intestine. Gharpure and Saldanha noted in their autopsy series that the large intestine 'showed no pathological condition' in 18.9 per cent of the cases.

Table 11: Site of intestinal ulceration

Site	No. of cases	Percentage
Whole of large intestine—from caecum to rectum	24	30
Caecum alone	8	12
Caecum and ascending colon	8	12
Ascending colon	8	12
Pelvic colon and rectum	1	4.5
No ulceration in large intestine	15	23.5

It is found that concurrent ulcers have been more common in the proximal portion of the large intestine than any other. This finding goes well with the theory which ascribes the occurrence of amoebic liver abscess more commonly in the right than in the left lobe to the fact that the portal circulation is made up of two currents the blood draining the proximal half of the large intestine chiefly circulating through the right lobe while that draining the distal half going chiefly to the left lobe.

Table 12: Site of perforation of the abscess at autopsy

Site	No. of cases	Percentage
Peritoneal cavity	10	40
Right pleural cavity	0	20
Right lung	2	0
Stomach	1	4.5
Both peritoneal and pericardial cavities	1	4.5

Cause of death as determined at autopsy is shown in Table 13

Table 13: Cause of death

	No. of cases	Percentage
Perforation of the abscess	21	31.0
Extensive destruction of liver parenchyma	14	21.2
Perforation of intestinal ulcer	0	0.2
Secondary lobar pneumonia or broncho-pneumonia	0	0.2
Active pulmonary tuberculosis	4	0.2
Miscellaneous	15	22.8
Total	60	

During the same ten year period i.e. from 1935 to 1944 amoebic intestinal ulceration was detected in 235 out of the 3946 autopsies performed giving an incidence of 6 per cent. This is about three and half times more common than amoebic liver abscess. Among the fatal cases the incidence of liver complication is bound to be high, but on the whole it is said to occur in only about 2 per cent of the cases of intestinal amoebiasis.

Perforation of the abscess found at autopsy

Perforation had occurred in 21 cases. The sites of perforation had been as shown in Table 12.

In the 15 miscellaneous cases the finding of the abscess was incidental and death was due to such varied conditions as multiple injuries, congestive cardiac failure, meningococcal meningitis etc

Conclusion Though quite a preventable condition, the amoebic liver abscess is found in one case out of every 1000 cases admitted to the hospital and in approximately one out of every 60 unselected autopsies, and though a readily curable disease especially in its earlier stage of 'hepatitis' the fatality rate is as high as 29 per cent largely due to the patient not coming in for treatment early enough or due to the condition being not suspected and diagnosed early enough

SUMMARY

- 1 An analysis of 130 cases of amoebic liver abscess diagnosed at the K E M Hospital from 1-1-1935 to 31-12-1944 is presented
- 2 Autopsy findings of 66 cases have been recorded
- 3 A marked preponderance of the disease is noted in the males
- 4 Majority were between the ages of 30 and 50 years
- 5 The disease has been found to occur without some patient, giving a history of previous dysentery or without concurrent ulcers in the large intestines in some autopsies
- 6 Roentgenography and exploratory needle puncture are the most important aids in diagnosis
- 7 The closed aspiration therapy with emetine has been found to be more successful than open drainage and emetine, the fatality rate being less than half as much in the former (13.3 per cent as compared to 28 per cent in the latter)

(I thank the Dean of the K E M Hospital for permitting me to go through the case records)

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DISCUSSION

Dr A V Baliga wanted to know the number of Liver abscesses which at primary aspiration showed a secondary infection so that the treatment of the secondary infection could be instituted. In his opinion the high operative mortality in the case of Liver Abscesses occurred in cases where repeated aspirations had failed, the abscess cavity was large and the patients were in low condition. Another factor in the mortality was the occurrence of secondary infection after an operation.

Dr P Raghvan stressed the low incidence of Liver Abscesses in females. His opinion was corroborated by Dr J K Mehta who cited the figures in China where the incidence in females was low.

Dr R G Dhayagude enquired whether the post mortem diagnosis of amoebic abscess was made on the basis of naked eye examination or whether an attempt was made to find out amoebic in the scrapings of wall.

Dr D D Banker replying said that secondary infections occurred after repeated aspirations. In a large number of the present series bacteriological examinations of the abscess contents was not resorted to.

Critical Notes and Abstracts

THE SYMPTOMATIC TREATMENT OF BRONCHIAL ASTHMA IN INFANCY AND CHILDHOOD JEROME GLOSER, M D, Rochestor, New York (*American Practitioner*, 1-185-190) The management of asthma in young children is often most troublesome Detailed instruction is given in this paper

1 *Put the Patient to Bed* In his own bedroom, he will be protected from house dust, feather or kapok pillows, and other environmental allergens if the proper precautions have been observed

2 *Start a Cough Mixture* The use of any drug in an allergic child must be regarded as an experiment until it is determined whether or not the drug agrees My favourite cough mixture for an asthmatic child is

Codaine sulphate	0 25	gr iv
Ephedrine sulphate	0 40	gr vi
Glycerin	10 0	dr ii
Syrup of hydriodic acid		
Syrup of cherry a d s ad	120 0	oz iv

A teaspoon of this mixture may be administered every 3 or 4 hours to a child 3 years of age and upwards Proportionate doses may be given to smaller children

If one wishes to add to the expectorant effect of the above cough mixture, a few drops of fluid extract of ipecac may be added Ipecac may also be used alone as advocated by Ratner to produce vomiting and thus relieve asthma The retching induced appears to favour loosening and expulsion of mucous plugs in the tracheobronchial tree

3 *Start Nose Drops if Nasal Congestion is Present* These should contain a mild vasoconstrictor such as ephedrine or some similar preparation I prefer a 1 5 per cent solution of ephedrine sulfate in 10 per cent dextrose (aqueous solution) with 0 5 per cent chlorobutanol added as a preservative It is of the utmost importance that the drops be administered with the child in the dorsal (Proetz) or lateral (Parkinson) head low position

4 *Steam Inhalations* These are of little value in the summer (except in dry climates) but are often helpful during the winter when the air of the room may be exceedingly dry and irritating to the respiratory mucous membranes A volatile medicament should not be added to the boiling water

5 *Insert a Suppository containing Aminophylline* A child 3 years of age will easily tolerate a suppository containing 0 25 Gm ($3\frac{3}{4}$ gr) For smaller children the suppository may be slit lengthwise, although even a child a year old or younger will commonly tolerate the aforementioned dose The action of the suppository may be helped by the addition of a small amount of a suitable barbiturate The suppository may be repeated every 4 to 6 hours if necessary

6 *Oral Administration of Ephedrine* Ephedrine sulfate or hydrochloride by mouth in doses of 15 to 50 mg ($\frac{1}{4}$ to $\frac{3}{4}$ gr) may be used It may be necessary to counteract the stimulating effect of the ephedrine by means of a sedative

7 *Inhalations of Epinephrine Hydrochloride* If the child continues to wheeze this procedure may be tried. Epinephrine hydrochloride in a 1 per cent solution is commonly employed. After the use of the epinephrine aerosol it is advisable for the child to gargle or to swallow a little water. Throat or gastric irritation rarely occurs if this precaution is observed. Overdose of the aerosol must be avoided by not using more than 3 to 5 inhalations at a treatment.

8 *Epinephrine by Hypodermic Injection* If, in spite of the above measures, the asthmatic attack continues recourse should be had without delay to the hypodermic administration of epinephrine hydrochloride 1 : 1,000. The two most common errors in this procedure are

- (a) Too long a delay between the onset of otherwise unrelieved asthma and the hypodermic administration of epinephrine
- (b) Improper dosage of epinephrine

The tendency is to use too large a dose of epinephrine. An infant of 4 to 6 months may be started on 0.15 cc (2 minims). An average child of 3 years of age will be relieved in a moderately severe attack by 0.25 cc ($3\frac{1}{4}$ minims). It may be necessary to repeat the dose several times at intervals of 15 to 20 minutes.

Occasionally epinephrine in oil 1 : 500, because of its slow absorptive properties and prolonged action, is of great value in individual cases. It is important to be sure that the child is not sensitive to the oil used in the mixture, and that the syringe be absolutely dry.

In some instances where the child will not take or vomits oral medication and will not retain rectal medication, it may be advisable to administer sodium phenobarbital dissolved in the epinephrine hydrochloride solution for purposes of sedation in doses of 0.032 to 0.065 Gm ($1/2$ to 1 gr). Demerol (pethidine hydrochloride) has similar advantages.

If the child has not been relieved of the asthmatic attack by the measures outlined above, he may then be considered to be in "status asthmaticus."

It is extremely important to keep the child well hydrated. The secretions must be kept thin by plenty of fluids, parenterally administered if necessary, and by other measures such as the administration of potassium iodide, and the inhalation of carbon dioxide and steam or otherwise dampened air.

The single most useful drug in this condition is aminophylline intravenously. Pratt recommends a dose of aminophylline of 0.008 Gm per kg of body weight ($1/20$ gr per lb) combined with 2 cc per kg (1 cc per lb) of 50 per cent dextrose solution given slowly intravenously. This mixture may be repeated every 6 to 8 hours if effective. The aminophylline may be administered as it is supplied in the ampoule without the addition of anything else.

The oxygen tent, provided the atmosphere is kept sufficiently moist, should be used in severe or prolonged asthmatic attacks without waiting for the child to show clinical evidence of cyanosis.

Penicillin aerosol has some merit at times, particularly in those cases where the asthma is related to pulmonary infection, but the long-term results are seldom striking.

As suggested by Holt for the prophylaxis of recurrent upper respiratory infections commonly followed by asthma sulfadiazene administered orally in the same manner that the drug is used for the prophylaxis of rheumatic fever has been helpful in a limited number of cases

The newer antihistaminics, benadryl and pyribenzamine valuable as these drugs are in other allergic conditions have been disappointing in my experience in asthma

RESULTS OF HIGH CALORIC FEEDING JOSEPH I GOODMAN AND ROBERT O GARTIN (*Gastroenterology* 6 537-562, June, 1946), became interested in the importance of diet during observation of a soldier admitted in stupor a month after receiving a severe wound in the right leg Examination revealed gas gangrene in the stump of a low thigh amputation Sepsis was controlled by reamputation, but anemia and generalized edema remained and recovery seemed doubtful This clinical picture plus a blood nonprotein nitrogen level of 180 mg per cent and creatinine level of 5 mg per cent suggested presence of the hepatorenal syndrome An intensive feeding program was instituted and after four weeks the patient was well

Following this experience the authors inaugurated a program for malnourished patients which entailed feeding 5,000 calories a day in three meals plus hourly feedings from 8-00 a m to 9-00 p m The diet contained 600-800 Gm carbohydrate, 150-250 Gm protein and 150-250 fat They report results of this feeding program in 78 malnourished soldiers

Liquids were often avoided because of their great bulk In these cases, powdered milk plus sugar, eggs and vanilla was used instead of whole milk Oral feeding was preferred to parenteral feeding for the same reason Although 80 Gm protein and 1,600 calories can be administered parenterally by use of protein hydrolysates, two ham sandwiches and two glasses of eggnog provide 96 Gm protein and 1,884 calories A typical daily schedule is contained in the table

The authors found it necessary to have a member of the dietary staff present at each feeding period to insure consumption of the food provided A record was kept of the exact amount of food consumed by each patient Patients were weighed daily and a graph made of daily weights Anorexia, nausea and even vomiting frequently made it seem impossible to force such large quantities of food After 18 hours of forced feeding, however, these complaints usually disappeared Anorexia was thought to be result of starvation in many cases The vicious circle of starvation and anorexia was broken by the insistence of medical department and encouragement of fellow-patients on the same dietary program

Average weight gain of the 78 patients during hospitalization was 14½ lbs Convalescence was accelerated, average period of bed rest for patients with hepatitis being 30 days On the first day out of bed these patients were assigned ward details and a week later sent to rehabilitation wards to take part in the full program preparatory to duty They were impatient to get to work, were surprisingly strong and did not experience fatigue

TYPICAL DAILY MENU SCHEDULE

Time	Food			P	C	F	Cal	
0800	Breakfast	Fruit juice	150 c c	0 6	10 6	0 1	70 0	
		Milk	100 c c	3 5	4 0	3 0	60 0	
		Bran flakes	30 Gm	3 0	21 4	0 6	103 0	
		Sugar	25 Gm		25 0		100 0	
		Eggs, scrambled	2	12 8	0 8	11 0	150 0	
		Bacon, 2 slices	15 Gm	3 0	0 2	9 8	101 0	
		Coffee, milk & sugar	25 Gm	2 2	28 0	2 4	142 0	
		Bread and butter	40 Gm	3 2	20 8	0 3	180 0	
0900		Sandwich, bread, -butter jam & peanut butter		10 4	60 0	17 3	478 0	
1000		Malted Milk and cake	100 c c	10 3	50 8	17 4	300 0	
1100		Pineapple, sliced	100 Gm	0 8	42 2	0 2	174 0	
1200	Dinner	Ham	90 Gm	18 3		20 1	254 0	
		Potatoes	100 Gm	2 0	10 1	0 1	85 0	
		Peas	100 Gm	3 3	10 1	0 2	55 0	
		Pear, canned	75 Gm	0 8	27 0	0 1	112 0	
		Bread and butter	40 Gm	8 2	20 8	0 3	180 0	
		Coffee, milk and sugar	25 Gm	2 2	28 0	2 4	142 0	
1300		Malted Milk	100 c c	0 8	18 0	0 1	103 0	
1400		Sandwich bread butter & corned beef		22 0	41 0	17 2	413 0	
1500		Eggs hardboiled	2	12 8	0 8	11 0	150 0	
1600		Sandwich bread butter & chicken		21 2	41 0	15 0	894 0	
1700	Supper	Meat loaf	85 Gm	10 7		0 5	187 0	
		Lima beans	100 Gm	7 5	28 5	0 8	181 0	
		Asparagus	50 Gm	0 0	1 5		10 0	
		Bread & butter	40 Gm	3 2	20 8	0 3	180 0	
		Cake	75 Gm	3 4	82 3	8 3	218 0	
		Cocoa	100 c c	18 2	88 0	17 1	361 0	
1800		Peaches, canned	100 Gm	0 4	18 2	0 1	75 0	
1900		Sandwich, bread butter & jelly		6 4	55 8	10 1	850 0	
2000		Egg nog	100 c c	9 8	18 0	0 1	193 0	
2100		Malted Milk	100 c c	9 8	18 0	0 1	193 0	
Total				213 0	713 5	220 1	5805 0	
CA	P,	Fe	VIT A	THIAMINE	RIBOFLAVIN	NIACIN,	ASCORBIC,	VIT D,
Gm	Gm	Gm	I U	MCG	MCG	MG	MG	I U
2 3 4 3		42	10013	4400	7850	78	114	278

The importance of food intake is often overlooked in surgical patients in whom weakness and weight loss are accepted as normal sequelae of operation or injury. That inadequate nutrition following operation may cause death by starvation is demonstrated by the following case.

A soldier was hospitalized after a shell wound in the abdomen. Part of the liver had been shot away, and multiple perforations of the intestine necessitated resecting of parts of both large and small intestine. Life was preserved by prompt surgery and maximal use of plasma and whole blood. During the first five postoperative weeks lavish use of blood, plasma and glucose maintained the electrolyte balance of the body despite anemia, sepsis, thrombo-phlebitis and decubitus ulcer. However, during this period he lost 50 lb, had marked mental depression and seemed moribund. Calculations revealed that parenteral feedings

had provided only 291 calories a day during much of this period. The feeding program described in this article was instituted and the patient recovered.

Use of a high calorie diet in patients with malaria has demonstrated that free administration of food does not raise body temperature and that absorption of large amounts of food is possible in the presence of fever. Increased metabolism resulting from the fever of typhoid has been shown to increase calorie requirements to 3,600-5,000 a day. The authors suggest that physicians have not applied their knowledge of metabolism to treatment of febrile illness because of fear of incurring the animosity of the sick patient, to whom the sight of food is repulsive. Study of a series of malaria patients revealed average weight loss of 10-12 lb, losses of over 20 lb, being common. The response of postmalaria headache, dizziness, anorexia, backache and nervousness to the 5,000 calorie feeding program demonstrated that these symptoms resulted primarily from malnutrition.

Amelioration of psychiatric symptoms was seen in a large percentage of a group of patients with psychoneurosis when general health was improved by high calorie feeding.

Three patients with idiopathic ulcerative colitis showed clinical remission and reversion to a normal proctoscopic appearance on 5,000 calorie feedings. Diarrhoea ceased within 48 hours in one patient with amebiasis after institution of the author's feeding regime, and weight gain was accomplished in peptic ulcer patients undernourished as the result of ulcer regimens.

THE TREATMENT OF MIGRAINE by H. T. ENGELHARDT, M. D. AND V. J. DERBES, M. D. (*American Practitioner*, March 1, 1932 395)
One of the most perplexing problems that the practicing physician has to face is the treatment of the migraines.

It is common information that many women have the attacks with or just before their menstrual period. It is also known that the intensity and frequency of the attacks may decrease or disappear completely during pregnancy and after the menopause. Since there is no constancy in the relation of headaches to the menstrual period varying hormones have been used. For example some individuals recommend the use of 1,000 to 50,000 I. U. a week of estrogenic substances. Because of the known relation of the pituitary gland to the ovarian hormones of the gonadotrophic hormones of the anterior pituitary have been used. The judicious use of thyroid extract in women who have a low basal metabolic rate is of real value. The use of female sex hormones in treating males with migraine has its advocates.

Perhaps one of the most widely held conceptions regarding the cause of migraine headaches is that it is on an allergic basis. Skin tests have their proponents, but it is well known that the accuracy of these tests in determining food allergy is by no means that obtained in testing for pollen sensitivity. When the requisite information cannot be obtained in this manner recourse may be had to the use of elimination diets and food diaries. Perhaps the simplest of the elimination diets is that of Alvarez which is composed of lamb, pear and rice. The patient adheres to this diet for 1 week and if at the end of this time the headaches still persist, it is unlikely that they are allergic in origin.

It has long been known that sedatives are of real value, either alone or preferably combined with ergotamine. The administration orally of ergotamine tartrate in 1 mg (gr 1/64) tablets is effective principally as a preventive measure. Usually the patient can anticipate an attack and if he is then given ergotamine tartrate, the episode can frequently be aborted. If the attack has developed, this medication must be given parenterally. The usual dose is 0.5 cc of 1:2,000 solution. Although this is frequently accompanied by nausea and occasionally by severe vomiting, it has been very effective in our hands in terminating an attack. One must always emphasize to the patient the danger associated with repeated injections of this medication. This is particularly true when a large number of tablets for oral administration are prescribed. The danger of ergot poisoning is a very real one and many individuals have developed gangrene of the extremities from improper administration of this drug. The basis for the gangrene is marked vasoconstriction which manifests itself by tingling and blanching of the extremities. If these symptoms do not occur one is justified in using the drug 2 or 3 times a week.

Histamine will at times benefit these individuals. It has been recommended that its use be confined to those individuals who are skin-sensitive to it. One may give it twice a week subcutaneously in increasing doses, starting with 0.1 cc and administering it over an interval of 3 or 4 months. Histamine azo protein (marketed under the name Hapamine) has definite possibilities. The initial dose of Hapamine is 0.05 cc and it may be increased at 3- to 7-day intervals until 1.5 cc is given.

We have used, with occasional dramatic success, inhalations of oxygen either as 100% or in combination with carbon dioxide. This form of therapy has its best effect when given early. It is important that when giving oxygen and oxygen-carbon dioxide combinations proper masks be used so that optimum concentrations may be attained.

Various vitamin preparations have been used from time to time, particularly thiamin hydrochloride, but we feel these are of little or no value.

No examination of an individual with migraine is complete without a detailed inquiry into his life and habits because frequently on the basis of information derived from these questions can one offer suggestions which may help decrease the incidence of the headaches.

- I Put the patient to bed and loosen garments
- II Darken quiet, well ventilated room
- III Apply ice cap to area of pain
- IV Use Oxygen inhalation when feasible. This relieves 10 per cent
- V Administer ergotamine tartrate
 - 1 Dosage Schedule
 - Intravenous administration 0.25 mg
 - Subcutaneous administration 0.5 mg
 - Oral administration 1.5 mg
 - Keep dosage to minimum consistent with relief of patient
 - 2 Side actions of ergotamine most common after intravenous administration
 - A Nausea and vomiting is the rule. After injection, these may be minimized with gr₁₆₀ - gr₁₆ atropine

- B "Muscular" cramps may appear along the course of the main arteries of the arms and legs Massage
- C Temporary paresthesias are frequent
- D Persistent paresthesias contraindicate ergotamine
- E No more than six injections per month
- 3. Precautions with ergotamine
 - A No more than 0.25 mg intravenously in one dose, no more than two such doses daily
 - B No more than 0.5 mg subcutaneously, no more than two such doses daily
 - C No more than 11 mg orally daily
 - D No more than two injections per week
- 4. Contraindications to ergotamine
 - A Septic states
 - B Obliterative vascular disease, especially coronary artery disease
 - C Incipient ergotism
- VI In protracted cases associated with nausea and vomiting glucose and saline infusions may be given
- VII Narcotics are contraindicated, but sedatives are helpful

Book Reviews and Notices

THE 1946 YEAR BOOK OF ENDOCRINOLOGY, METABOLISM AND NUTRITION
 Edited by WILLARD O THOMPSON, M D (ENDOCRINOLOGY) and TOM D SPIES, M D (METABOLISM AND NUTRITION) 1947 YEAR BOOK PUBLICATIONS, 304, South Dearborn Street, CHICAGO (U S A) 85 Illustrations 573 pages Price \$ 3.75 Size 18 x 13 cm

In the past the section of Endocrinology was a part of THE YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND ENDOCRINOLOGY. This year it is published in a new year book, together with a section on Metabolism and Nutrition. The appearance of a large number of papers on these subjects during recent years justifies the venture of the publishers in devoting a new volume to them. As is usual with this series of Year Books, in the selection of articles for abstractions the editors have kept the needs of the general practitioner in mind, as well as the more important scientific advances. The newer antithyroid drugs have established their value in clinical medicine and there are many articles dealing with Thiouracil, Methyl thiouracil, Propylthiouracil, Aminothiazole, and Radio active Iodine. There is little doubt that testosterone propionate a valuable and potent therapeutic agent is much abused in practice, articles dealing with its indications and untoward symptoms produced by its use are welcome. Hans Selye's views on General Adaptation Syndrome and Diseases of Adaptation are highly suggestive and throw new light on many clinical states and therapeutic measures. Spies firmly believes that Folic acid (synthetic *Isotobacillus casei* factor) has established its value in macrocytic anaemias and in sprue. Paraaminobenzoic acid is recommended in Rickettsial diseases, with an initial dose of about 8 Gm, followed by 3 Gm every 2 hours until a blood level of 30-60 mg per 100 cc of blood is reached.

PENICILLIN THERAPY: also includes other ANTIBIOTICS LIKE STREPTOMYCIN, by J R GOYAL 2nd Edition 1947 Published by Himself Pp 177 19 x 13 cm Price not mentioned

The appearance of a second edition in a short period of two years shows the usefulness of this compilation. The matter is brought up to date and a chapter on other antibiotics, e.g. Streptomycin is added in this edition.

FOOD AND NUTRITION IN INDIA: Edited and published by DR D N CHATTERJEE, 3/2, Colleges Street, CALCUTTA 235 Pp Size 18 x 14 cm Price Rs. 6/-

The book is divided in two parts, the first dealing with the fundamentals of physiology of nutrition and the second with Food and Nutrition. All known facts are presented in a simple lucid way to make it intelligible to general readers. We have no doubt the book will prove useful to social workers, school masters, and heads of institutions, etc. Medical practitioners may recommend it to their patients who are anxious to acquire basic knowledge about diet and nutrition.

Our Problems a forum for discussion

A LESSON FOR THE PRESENT GOVERNMENT IN THE REGISTRATION OF AYURVEDIC PRACTITIONERS by S B GADGIL In the year 1943-1945, the General Assembly of Tennessee in America passed a law legalising the licensing of naturopaths. In the same years the Government of Bombay passed a law to register Unani and Ayurvedic Medical Practitioners. A Board was established in Tennessee to deal with such licensure. Within a week after the law was passed, a notice was sent all over America that the Board issues licenses in Tennessee to naturopathic healers and Tennessee became a hunting ground for such healers. A Board of Naturopathic healers met in Nashville four months later and hundreds of licenses were issued like tickets to a banquet. It is estimated that about 1,500 licences to practice naturopathy were doled out to those who could purchase them. A political organisation was established for the maintenance of this unfortunate system of practice. One of the Naturopaths went so far as to practise ordinary system, prescribed 4 ounces of Sulphate of iron for high blood pressure which the patient did not have and was fined 500 dollars and a year's imprisonment. The scandals of this practice went so far that the Authorities abolished this Board for licensing naturopaths, but one does not know how long Tennessee and the rest of the United States will be paying for the folly of the Assembly in 1943 and 1945. We, in India, will also have to pay for the folly of our legislature in registering all kinds of people as Unani and Ayurvedic Practitioners, who know about the constitution of human body no more than those naturopaths and are issuing drugs and methods of treatment only to be learnt by regular attendance at Medical Schools and Colleges. We have gone in our folly still further by establishing schools to teach these old systems based on theories and crude observations proved to be incorrect and fallacious by scientific methods ranging over 200 years. One expected at different treatment to these Unani and Ayurvedic practitioners from a Minister well versed in the Western System of Medicine so as not to allow these charlatans to flourish under Government protection. I wonder if the Government of Bombay will see its folly like the Tennessee Assembly and convert these Ayurvedic and Unani Schools in institutions teaching modern and up-to-date Medical Science for the want of which these Naturopaths, Homeopaths, Unani Hakims and Ayurvedic Vaidyas seem to flourish. The number of these pseudo-qualified registered men is over 4,000 already.

News and Notes

Surgical History from Pre-Historic Days By LINCOLN WALLACE—Examples of Hindu, Assyrian, Babylonian, Chinese and classical Greek and Roman surgery were on view at an exhibition in London recently of books and instruments illustrating the history of surgery. The display was arranged by the Wellcome Historical Medical Museum, from which all the exhibits came, in connection with the 12th Congress of the International Society of Surgery.

One section showed the development of surgery from its earliest beginnings and another was devoted to a selection of specialised forms of surgery, including cranial, abdominal and plastic surgery, neuro surgery, lithotomy, ear, nose and throat surgery and ophthalmology. Included in this latter section was a group showing the development of various types of surgical instruments.

In the historical section, evidence was presented that there were surgical operations performed even in prehistoric times and the exhibits included illustrations of a trephining operation in France 4,000 years ago—the object of which was probably, in the custom of primitive races, to let out the evil spirits with which the man was afflicted.

Rare Manuscripts An example of the many sets of Roman surgical instruments which have been discovered was on view—a fine set of about 50 instruments in bronze and copper, dating back to 50 B.C. Other exhibits took the visitor through the period of mediæval surgery and those of later times including those of William Harvey, the Hunters, Pasteur and the germ theory and led up to a section on Lister's introduction of the antiseptic method. Many illustrations, drawn from old treatises, were displayed, as well as some fine manuscripts and a selection of the most important books, including the first edition of William Harvey's *De Motu Cordis* in which he described the circulation of the blood.

A particularly interesting exhibit consisted of one of the few known examples of a luxation table, for reducing dislocations by stretching and manipulation. This dated from the early sixteenth century and was found in a monastery where it was being used as a refectory table. (*British Information Service*)

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Original Contributions

ENTERIC FEVER

A PRELIMINARY REPORT ON THE INVESTIGATION AND TREATMENT

by

J C PATEL

L MONTEIRO

D D BANKER and

MISS B P KAPADIA

A special ward of 9 beds—6 males and 3 females in the King Edward Memorial Hospital, Bombay, was opened on 1st November 1946 for the investigation and treatment of enteric fever. Patients were admitted under the care of one of us (J C P)

The procedure adopted with those admitted to this ward was as follows —

Fluoroscopy of the chest is carried out before the patient is brought to the ward, or if not, then it is done soon after admission, provided the patient's condition permits. Immediately on admission, the nurse on duty sends a call to the house-physician. The house-physician (B P K) on receiving the call attends to the patient at once, examines him and writes complete notes incorporating the following details—

The following symptoms are specially inquired into

Cough, headache, sleeplessness, constipation, frequency of stools, vomiting, pain in the abdomen, epistaxis, pain in the back and joints, pain in the chest, anorexia, deafness

The history with special regard to the following is obtained

The nature of the onset, malaise before the fever started, treatment at home especially with purgatives or quinine, previous fever, T A B inoculation, contact cases

The following signs are carefully looked for

The typical typhoid tongue, palpable liver or spleen, tenderness or distension of the abdomen, roseolar rash on the abdomen, chest, or back, bronchitic signs in the chest, slow pulse rate, signs of general toxicity and presence of any complication

One of us (D D B) collects the various materials for the following investigations —

(1) Blood for —

(a) Blood culture—the cultural examination of the blood is carried out on admission regardless of the duration of the fever

(b) Clot culture

A paper read before the 71st meeting of the Seth G S Medical College and K.L.M. Hospital Staff Society held on 13th June, 1947 with Dr. N. D. Patel in the chair

- (c) Total and differential w b c count
- (d) Peripheral smear examination for parasites
- (e) Widal reaction—both H and O agglutination
- (ii) Urine for
 - Routine examination, which in most cases is confined only to albumin, sugar and microscopical examination of the deposit
- (iii) Sputum—if necessary
- (iv) Urine for culture } if the duration of the fever is more than two weeks
- (v) Stool for culture }

If the patient is admitted during the first 2 weeks of fever, the urine and the faeces are cultured later as soon as he reaches the 15th day of fever and subsequently repeated every 7 to 10 days (These investigations were carried out by L M and D D B)

Special investigations like culture of the bone marrow or of the material from rose spots were carried out only in isolated cases

If the patient at any stage of the investigations is found to suffer from disease other than enteric fever, he is transferred to the general wards. In other cases of fevers, the investigations are pursued further. In every case detailed notes of the progress of the patient are written out by the house-physician

The total number of cases admitted during the seven months from the inception to 31st May 1947 has been 100. All of these were suspected to be enteric fever. After investigation, the incidence of various diseases has been found to be as follows —

49 cases did not belong to the enteric fever group. They comprised the following diseases —

- Malaria 0
- Typhus 0
- Pyelitis 7
- Pulmonary tuberculosis 4
- Inf hepatitis 2
- Meningitis 2
- Interstitial bronchopneumonia 2
- Pleurisy with effusion 1
- Pneumococcal septicaemia 1
- Short fever with mepacrine psychosis 1
- Cholaemia 1
- Pyrexia of unknown origin 10

37 cases could be proved bacteriologically to be definite cases of typhoid. Of these, in 36 the blood culture (either whole blood or blood clot) was positive, while in 1 the urine culture was positive associated with an O agglutination titre of 1 in 250. In the remaining 14 cases, the blood culture was negative, but other positive investigations and the clinical course appeared to be in favour of the diagnosis of enteric fever. Of these

- (a) 2 cases gave positive stool cultures but with other cultural investigations negative and a low O agglutinin titre
- (b) 2 cases showed a rising O agglutinin titre
- (c) 4 cases gave an O agglutinin titre of 1 in 125 or more
- (d) 1 case showed rising H agglutinin titre
- (e) 5 cases gave an H agglutinin titre of 1 in 250 or more one of these was positive for B paratyphosus A only

Thus a total number of 51 enteric cases were met with, in 37 of which the causative organism was isolated. The remaining 14 were serologically positive. In one of these, agglutinins against B paratyphosus A only were detected.

The percentage error in diagnosis is 49%, 49 cases out of the 100 being definitely not enteric. Rolleston (1940) gives a percentage error of 46.4% amongst his series in England. Dhayagude (1937) reported autopsy records of 12 cases clinically diagnosed as enteric in which the diagnosis was erroneous in 7 cases, among the diseases mistaken in his series as enteric were malaria, lobar pneumonia, amoebic liver abscess and syphilitic meningitis.

A brief review of the 37 culture positive cases is now given.

(a) 36 were clinically typical, 1 was atypical, the patient being ambulatory throughout the course.

(b) General build could be described as good in 11 cases and average in 26.

(c) Previous T A B inoculation was carried out in only 2 cases—in both within one year of the onset of the disease.

(d) Treatment with purgative and quinine during the first week seemed to produce adverse effect on the subsequent course of the disease. We understand that other observers have reported similarly.

	Total	Recovered	Died
Purgative	11	7	4
Quinine	6	2	4
Others	20	18	2

(e) Community—Hindus 23
Christians 14

Absence of the other communities is probably due to the civil disturbance during the period, the Hospital being in a Hindu locality.

(f) Age—The cases have occurred mostly among young adults.

Up to 15 years—5 cases—youngest aged 8 years.

15 to 30 years—26 cases.

Above 30 years—6 cases—the oldest in the series being 35 years of age.

(g) Sex—Male 20 female 8.

(h) Monthly incidence—

Nov	Dec	Jan	Feb	March	April	May
5	2	4	6	6	5	9

(i) Duration of fever at the time of admission.

Within first week—7 cases.

During second week—21 cases.

During third week—8 cases.

During fourth week—1 case.

Thus it is seen that positive blood cultures were obtained in 9 out of the 37 cases primarily after the second week.

(j) Contact cases.

History of contact with another case (or common source) could be obtained in 7 cases. Of these there were 2 married couples, 1 brother and sister, and one a priest in whose school there had been another case.

The occupational incidence and the incidence of symptoms and signs have been worked out, but are not presented here for the sake of brevity. In passing, an important sign may be emphasised, viz the rose spots which were found in as many as 12 cases out of 37.

(k) Complications.

These developed in 24 cases while 13 cases ran a course without any complications. Of these 24, in 8 cases only minor complications like distension, abscess, bed sore, etc. developed, while 16 cases developed, together with some minor complications, one or other of the major complications like haemorrhage, perforation, pneumonia, hyperpyrexia, etc.

Major

Minor complications

Hyperpyrexia	6	Distension	8
Peripheral failure	6	Meningism	6
Pneumonia	3	Delirium	7
Intestinal haemorrhage	7	Stomatitis	4
Pulmonary oedema	4	Deafness	4
Pneumococcal septicaemia	1	Abscesses	2
Intestinal perforation	1	Otitis media	1

Major

Minor complications

Hiccough (persistent)	2	Alvcolar Abscess	1
		Laryngeal perichondritis (of right crico arytenoid joint)	
		Retention urine	1
		Petechial haemorrhages	1
		Jaundice	2
		Diarrhoea	5
		Bed Sores	4
		(2 admitted with them)	

(I) Laboratory Investigations

(i) Total white blood cells

Leukopenia—below 6,000/c mm was found in 26 cases. Of these the total count was below 4,000/c mm in 10 cases. The lowest met with was 3,100/c mm. 1 case only had above 10,000/c mm. 10 cases had between 6,000 to 10,000/c mm.

(ii) Differential w b c count. The usual finding was neutrophiles, lymphocytes and monocytes in normal proportions or there was some increase in the lymphocytes at the expense of the neutrophiles. Absence of eosinophiles in typhoid infection has been pointed out by many observers. Eosinophiles were found in only 3 cases out of 37, and in each case they were less than 4%.

(iii) Blood Culture

In 36 cases the blood culture was positive—either in whole blood or blood clot, or both.

Of these, 5 cases were positive only by clot culture—the whole blood showing no growth on prolonged incubation.

Both whole blood as well as blood clot culture was positive in 24 cases, while whole blood was positive with negative clot culture in 7 cases.

(iv) *Widal reaction*. H agglutination was carried out in 36 cases and found positive in 27 cases. On repeating, it became subsequently positive in two more cases. O agglutination was carried out in 29 cases and found positive in 23 cases. When repeated in 4 of the negative cases, it became positive subsequently. A diagnostic titre of O agglutination in a dilution of 1 in 250 was obtained in 15 cases. The highest O agglutination titre obtained has been 1 in 1250 in one case and a titre of 1 in 1000 has been obtained in several cases. A rising titre of O agglutination was obtained in 7 cases out of the 10 in which repeated tests were done. Vi agglutination was not carried out due to technical difficulties.

(v) *Urinary changes* indicating some kidney damage like presence of large number of pus cells, granular casts or red blood cells were found in 7 cases.

(vi) *Urine culture* was carried out in 20 cases out of which it was obtained positive in 3 cases. In 6 cases repeated urine cultures were found to be negative.

(vii) *Stool culture* was carried out in 30 cases out of which it was found positive in 2 cases while in 18 cases it was repeatedly negative. In two cases we observed positive stool culture only, failing to isolate the organisms by other cultural methods.

TREATMENT

The culture positive cases which totalled 37 were treated by two different methods, viz

- (i) The intramuscular use of massive doses of penicillin combined with oral administration of sulphathiazole and,
- (ii) The use of specific stock bacteriophage. A third of the cases were left as controls in strict rotation in the later period.

That the combination of penicillin and sulphathiazole has a pronounced bactericidal effect on *B typhosus in vitro* was shown by Bigger in the early part of 1946. He suggested the institution of treatment in enteric cases with combination of sulphathiazole and penicillin. Penicillin should be given preferably by continuous administration at the rate of 2½ to 3 million units per day so as to maintain a concentration of over 2 units per cc in the serum. Sulphathiazole should be administered in full doses to reach the blood level of 10 mgm/100c c. This treatment should be continued for at least five days and preferably for seven days. Subsequently, cultures for *B typhosus* from body

fluids (blood, faeces or urine) should be taken and if positive and treatment should be resumed for 4 days

McSweeney (1946) treated 5 cases of severe enteric fever according to the suggestion put forward by Bigger, 4 of these were bacteriologically proved by the isolation of *B. typhosus* from the blood. The fifth was clinically enteric with strongly positive Widal reaction and *B. typhosus* was isolated from the faeces and the urine. The dosage evolved by trial was a loading dose of 2 gms of sulphathiazole followed by 1 gm 8-hourly and 200,000 units of Penicillin 2-hourly until a total of 34 gms of sulphathiazole and 10 million units of penicillin had been given over a period of 4 days. Four cases were treated with the above combination. Two courses of 4 days each were given. He found speedy disappearance of toxæmia, subsidence of pyrexia and disappearance of the organisms from the blood, faeces and urine at the end of the second course in three of the four cases.

The dosage followed in this ward is slightly different. An initial dose of 2 gms of sulphathiazole is given followed by 1.5 gms 4-hourly day and night for five days. Penicillin, 200,000 units is given intramuscularly every two hours until a total dosage of 10 to 12 million units is administered.

At first, the locally prepared bacteriophage, which was originally isolated by Dr Dhayagude from the Dadar Sewage in 1942, was intended to be used orally, but in the meanwhile an article published recently in 1946 by Knouf and others indicated the marked beneficial effect of intravenous administration of type specific bacteriophage. They treated 56 cases with type specific phage—the method of administration being a single dose of 1 c.c. of phage diluted in 500 c.c. glucose saline and given by intravenous drip, taking about 5 hours to run in. This led to a moderate chill starting 1-2 hours after the commencement of the therapy and lasting 30 minutes. The temperature then rose to 105° to 107°F° (rectal) and later touched normal in 9 to 24 hours and in most cases remained normal. In some cases the therapy required to be repeated. The mortality in their series has been only 5%. These 56 cases were all blood culture positive before the treatment. The majority of the patients achieved a cure by crisis according to the following criteria:—

- (a) Negative blood culture in 24 hours after treatment and continuously negative thereafter
- (b) Absence of fever after treatment and
- (c) Immediate clinical improvement

These results were striking enough to prompt us to try our bacteriophage by the intravenous route. After adequate animal tests it was decided that the bacteriophage was safe for intravenous use and it is at present used by that route whenever it is employed.

In the beginning we did not try to treat the patient that appeared to be mild cases, keeping them as controls—hoping that the next case would be a fairly serious one on which a therapeutic trial would be worth while. But this led to an unmanageable number of controls. Hence, for the last 3 months we take up every third case in strict rotation for penicillin or phage treatment, or as control whether the particular case is mild or severe. At the completion of either treatment, blood culture is repeated in every case.

The Diet

Every patient is given a basic diet consisting of 120-150 ozs of fluids per day including milk, tea, fruit juice and water. He gets about 40 ozs of milk or butter milk, 12-16 ozs of fruit juice, 16 ozs of tea, egg preparations and as many bananas as he can take. The same diet was given successfully in 2 cases that developed haemorrhage. If diarrhoea or distention develops the only change in diet made is that milk is changed to buttermilk and fruit juice stopped, but the solid food is continued unchanged. It has been our practice to encourage patients to drink large quantities of fluids. As regards caloric value of the diet, no fixed rule is followed. The quantity and quality of the food depends upon the desire and inclination of the patient, the above provides between 1000-1500 calories. Injections of glucose, calcium or any other drugs or vitamins are not given. If the patient is toxic and does not take enough by mouth, glucose saline 500 to 1000 cc by subcutaneous or intravenous route is administered. Blood transfusion is given where indicated.

As soon as the patient feels better and starts taking interest in his surroundings he is encouraged and coaxed to take the full diet even though he is running a temperature. With the intake of diet it has been observed that the general condition of the patient improves considerably and temperature shows a downward trend. In no case have we found a relapse being induced by the diet. The patient is able to sit up in bed within a day or two of his temperature becoming normal and is able to walk about the eighth day of convalescence. In a majority of the cases the weight of the patient is only very slightly less than that previous to the attack. One of our cases was able to attend to his strenuous duties on the 16th day of his temperature becoming normal and at that time his weight was only 2 lbs less than his previous weight.

RESULTS

The fatality rate among the 37 culture-positive cases has been 27% (10 out of 37) and among the 51 possible enteric cases it has been 21.5% (11 out of 51). Out of the 10 deaths in culture positive cases, causes of death were —

- 4 cases died of hyperpyrexia and peripheral failure
- 2 cases died of intestinal haemorrhage
- 1 case died of perforation
- 2 cases died of pneumonia with pulmonary oedema
- 1 case died of pulmonary oedema and typhoid toxæmia with pneumococcal septicaemia

Treatment	No of cases treated	Cured Cases				Died
		Temp normal in 48 hours	Course of fever altered favourably	Course of fever not altered favourably	Total	
Penicillin & Sulphathiazole	13	2	7		9	4
Bacteriophage	9	2	8	2	7	2
Control	15				11	4

Lentin (1933) observed two and a half times higher mortality (82.85%) amongst the cases with positive cultures as compared to the culture negatives (18.05%) and also mentioned a bad prognosis in cases where the organisms persisted in the blood for a long time. Minchin (1939) also observed a higher mortality among the culture-positive cases. A fair number of cases were admitted directly to our ward, but a number of typhoid cases where culture was positive were transferred from general wards to this ward, whereas the milder culture negative but serologically—positive cases were kept and treated in the general wards only. Thus, the majority of our selected cases were of a serious nature. The higher mortality amongst our series as a whole and particularly among the selected culture positive cases may be due to the above reasons. Out of the ten cases, one died within three hours of admission and another who was admitted in a very toxic state died 4 days after admission before the culture report was available. Both these cases died of haemorrhage.

RESULTS OF PENICILLIN TREATMENT

Penicillin with suphathiazole treatment was instituted in 9 culture-positive cases and penicillin alone in 2 culture-positive cases. In two of the former, the temperature touched and remained normal at the end of treatment. In two other cases the combined treatment brought the morning temperature down to normal, but it was 6-8 days before the evening temperature became normal. In one case penicillin alone had a similar effect.

In one case the 1st combined treatment had no effect and blood culture remained positive at the end of it. However, the 2nd course of 5 days succeeded in bringing down the temperature to normal. One patient who was severely toxic, rowdy and semi-conscious was administered the combined course. There was marked improvement in general condition, rowdiness and toxicity, but the temperature ran its course for 5 weeks before touching normal.

One female patient was given penicillin alone. There was marked improvement in the general condition and the temperature remained normal for a day. During the course of treatment she had abortion, diarrhoea and intestinal haemorrhage. Later she developed intestinal perforation and succumbed to it despite best of surgical aid. The husband of this woman who was warded simultaneously and kept as a control also died indicating the virulence of the infecting strain from the same course.

Two other cases who were given the combined treatment died of hyperpyrexia, one on the second day and the other on the 4th day of treatment. They were evidently severe cases and succumbed before the treatment was effective.

Another case died of pneumonia and pulmonary oedema during the course of treatment.

RESULT OF BACTERIOPHAGE TREATMENT

One patient was given bacteriophage orally, while 8 were given the phage by the intravenous route. The first, i.e., the orally administered case died of hyperpyrexia and peripheral failure during the second week of his illness. Out of those given intravenously, one died but he was subsequently found to have a combined typhoid and pneumococcal septicaemia, the latter developing as a complication of the former.

In two, the temperature came down to normal in the second week within 24 hours after the therapy and after a few slight reactionary rises settled down as shown in the temperature charts, resulting in a definite cure, the subsequent cultures being negative. The husband of one of the two cases described above, presumably infected with the same strain was treated as control and in his case the temperature dragged on for nearly four weeks.

In the other 5 cases, the temperature after touching normal went up again the following day and took its own course, though at a lower range. These failures may be due to the lack of availability of type specific phage, i.e. phage specifically active against the particular infective strain, thus necessitating at present the use of stock bacteriophage in every case. Even then, the blood culture did become negative after treatment in 8 cases and they recovered without any complications. These cases were all given 1 cc. of our stock bacteriophage diluted in 500 cc. saline by intravenous drip taking about 4 hours to run in. The expected reaction due to the lysis of the organisms, viz. rigor, occurred in 1-8 hours after commencement of the drip and was in some cases severe enough to throw the patient into temporary cyanosis and collapse. The temperature then rose to anything between 104°F and 103°F (axillary) and subsequently fell to 97°F in every case with a very beneficial change in the patient's physical and mental condition. Unfortunately in half the cases so far treated, this benefit has been found very short lived, the temperature rising the following day to almost the same level as before.

A few remarks may be made regarding hyperpyrexia, the largest single cause of death in this series—being responsible for 4 deaths. Actually, it occurred in 5 cases, out of which one could be saved. Peripheral failure also occurred in these five cases simultaneously with the hyperpyrexia and it appears that this dreaded complication is due to the hyperpyrexia—which may be prevented by timely and vigorous hydrotherapy.

SUMMARY

1 100 cases have been investigated out of which 51 were enteric cases, 87 of these being culture-positive.

2 The percentage of positive cultures has been much higher than recorded by other observers.

3 Rose spots were found to be present in 12 of the 87 cases.

4 In 9 cases bacteriophage treatment was tried, in only two cases there was the expected immediate improvement.

5 18 cases were given penicillin and sulphathiazole treatment. It was found beneficial in 9 cases, in two of which temperature touched normal in 48 hours.

6 By giving the diet early in the course of the disease and administration of adequate fluids from the beginning, there was a rapid progress in the convalescence and general condition of the patient.

7 There have been no relapses in the series.

8 In two cases of intestinal haemorrhage diet was continued throughout with beneficial results.

ACKNOWLEDGEMENT

We thank the Dean of the K.E.M. Hospital for giving us all facilities, Prof R. G. Dhayngude for suggesting the Bacteriophage treatment, the matron and her staff for nursing help and the Glaxo Laboratories Ltd., for generous supply of the penicillin used in this investigation, free of cost.

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DISCUSSION

Dr B B Yodh suggested that the concentration of 12 units of Penicillin for 100 c.c. of blood would inhibit the growth of *B. typhosus* in vitro. This concentration, he added, would be necessary in the treatment of the disease. He cited two cases treated by him with Penicillin (250,000 units, three hourly) where pyrexia was controlled on the 12th and 14th days.

Dr N D Patel said that there were three rational lines of treatment in typhoid—Felix serum, Bacteriophage and combined Penicillin Sulphathiazole as suggested by Bigger. The first was not available, whereas the other two were tried in the present series. He could not understand the high mortality in the series as compared to the accepted figures (10 to 12%) and suggested further work on the same lines. He also suggested a culture of the sternal marrow in blood negative cases and examination of the stool to detect the carriers.

Dr J C Patel replying to Dr Yodh said that the concentration of Penicillin in the blood might reach the figure quoted by him, but it was difficult to assert whether the same concentration would be obtained in the lymphoid tissue. Replying to Dr N D Patel, the speaker said that the higher mortality might have been due to the severe types of cases admitted to the special ward from the general wards of the Hospital. He added that sternal marrow cultures were attempted in three blood negative cases. As for the incidence of carriers, no patient was discharged till the stool culture was negative on three occasions at the interval of one week.

Clinical Case Reports

ACUTE MASTOIDITIS WITH SINUS THROMBOSIS AND LUNG ABSCESS

by

H B BHATT, M.S., F.C.P.S

Chief Medical Officer, L. W. Ashktashram, SURAT

On 8-7-47, Mrs G D aged 30, was admitted to the L W Ashktashram Hospital, Surat with the following history She had right sided otorrhoea for sometime and for the last twenty days was complaining of pain and tenderness in the right mastoid region She had a swelling in the mastoid region of a week's duration, which gradually spread to the right side of the neck and she was having fever with rigors

On examination the right mastoid region was excruciatingly tender on palpation and there was an inflammatory induration in the right side of the neck A firm cord like structure could be palpated in the line of the right internal jugular vein suggesting thrombosis of the vein On the day of admission she had temperature of 103°F in the morning which had come down to 98°F in the evening She had no facial weakness, no signs of labyrinthitis and no indication of a cerebral abscess

She had a dry cough and the chest on examination showed dullness in the lateral and posterior part of the right lower lobe On auscultation, there were showers of loud coarse rales in the region The right upper lobe and the left side of the chest were clear There was no other metastatic manifestation

A diagnosis of acute mastoiditis with sinus thrombosis and a metastatic abscess in the right lower lobe of the lung was arrived at It was further thought that the abscess still did not communicate with a bronchus as she did not bring up any expectoration

Before admission to the hospital, she was treated with about a million units of penicillin by a general practitioner

She was operated upon on 4-7-47 under open ether anaesthesia The usual post-auricular incision was taken to start with and the mastoid process was exposed The bone was found to be extremely sclerotic so much so that it blunted a gouge during operation The aditus was located and all the cells were systematically exenterated The dura of the middle cranial fossa as well as that of the posterior cranial fossa did not reveal any granulations suggestive of an extra dural abscess Attention was now turned to the Sinus and the sigmoid part was carefully exposed With a view to determine the condition of the Sinus, an aspiration was performed which withdrew pure pus It was now decided to tie the internal jugular vein on the right side and with that end in view, an incision of about 4" was taken along the anterior border of the right sterno-mastoid from the Sterno-clavicular junction upwards The internal jugular was exposed and a ligature was first passed behind it, almost at its junction with the Subclavian The vein was then incised and again pure pus came out from the cut vein Thinking that the thrombosis had spread even proximal to the termination of the internal jugular we passed a rubber catheter attached to suction apparatus and sucked away as much of the pus as we could The ligature, previously in place was then tied as low as possible The distal portion was then dissected off after cutting it beyond the ligature The incision was

extended right up to the mastoid tip and the common facial tributary was tied off. It was not thrombosed. The whole body of the vein was removed after placing another ligature on the vein just below the tip of the mastoid.

The mastoid incision and the incision in the neck were now joined and the outer circumference of the jugular foramen was nibbled away.

A posterior extension from the original mastoid incision was now made and the occipital bone was exposed right upto the external occipital protuberance. The exposure of the Sinus was now carried backwards and the whole transverse part was laid bare. It contained pus even here. The whole sinus was slit open and the pus was drained out. It was then packed. The wound was lightly sutured and a pack was brought out both at the upper and lower end of the incision in the neck.

The patient stood the operation well but was still running a temperature ranging from 100°F to 101°F in the afternoon. With a view to control the infection both in the operated areas as well as in the right lung, she was put on penicillin 40,000 units every three hours till 6-7-47 supplemented by Sulfadiazine tablets by mouth. From 7-7-47 she was given 200,000 units of penicillin in pendil and was further given Sodium benzoate by intravenous injection with glucose. The treatment was continued along these lines.

There was no response to treatment and the rise of temperature to 100°F persisted. The cough started becoming worse and now she brought up increasing quantities of evil smelling typical "lung-abscess" sputum. Thinking that we would not be able to secure a resolution of the lung abscess by conservative treatment, we decided to drain the abscess in two stages. A radiogram of the chest was taken on 18-7-47 and it showed a peripheral half-filled lung abscess with surrounding pneumonitis at the level of the 8th rib.

Incidentally, I consulted my friend Dr. L. H. Hiranandani, F.R.C.S., D.L.O., when I visited Bombay at this juncture, about the feasibility of a bronchoscopic aspiration and topical application of penicillin. His opinion also was that a two-stage drainage would be more suitable for this case than repeated bronchoscopic aspirations.

On 25-7-47 a resection of about 2" each of the 9th and 10th rib on the right side was performed in the post-axillary line under local anaesthesia. The neuro-vascular bundle was tied at each end and the muscles were peeled off from the pleura. The extra-pleural space was packed with a roller gauze soaked in iodine and the incision was loosely sutured. The pack was removed on 1-8-47 and an attempt was now made to locate the abscess by preliminary aspirations. No pus could be struck but foul smelling gas came out at one place and it was decided to make a small nick at that level. During this manoeuvre, air started getting sucked in the pleural cavity and we decided to stop at this stage as the adhesions were not sufficiently strong. The wound was re-packed and re-sutured.

On 8-8-47 another attempt was made to open the abscess, this time under fluoroscopic guidance and we could remove quite a quantity of pus. A big drainage tube was put in the pleural opening and a smaller one near the abscess cavity in the lung.

All during this time, the cough continued to be very severe so as to interfere with her sleep and the temperature persisted. Penicillin

was continued, occasionally sulfadiazine was given and once 12 cgms of sulfarsenol were injected. The cough was helped by a stimulating expectorant mixture and intravenous injections of sodium benzoate.

As the temperature persisted, the roof of the abscess cavity was cauterized on 24-8-47. The cough was now getting less and so was the amount of expectoration which had lost its foul odour. Quite a lot of evil-smelling discharge came out from the opening. Methylene blue injected into the abscess cavity was not coughed out, thus excluding a broncho-pleural fistula. Once we tried to irrigate the abscess cavity with a mild solution of Dettol but it was followed by a fever with a severe rigour and it was given up forthwith.

The temperature still persisted in spite of daily injections of penicillin and establishment of adequate drainage. As the patient was getting emaciated and severely anaemic, she was given a blood transfusion (150 cc) on 29-8-47. A radiogram of the chest was taken on 1-9-47 to study the condition of the lung on the operated side and to exclude the formation of another abscess.

The X-Ray showed thickening of the pleura on the affected side. The abscess cavity was empty with a track leading to it from below. There was no abscess on the opposite side.

The cough by now had considerably diminished and we put down pleural infection as the cause of pyrexia. It was decided to keep her continuously on penicillin from 3-9-47 giving 50,000 units every four hours. At about this time a broncho-pleural fistula was established.

The temperature still rose to 99°F in the afternoon but the duration of the rise gradually diminished. All other symptoms slowly regressed and the broncho-pleural fistula closed by itself. The wound went on becoming smaller and smaller till it was completely healed on 1-10-47. The temperature also came down to normal on 30-9-47 and the penicillin injections were stopped from 1-10-47. She was finally discharged on 6-10-47.

She reported after a week and was afebrile and had no cough. She was requested to report after a month and to inform earlier if there was any deterioration in her health.

Following points pertaining to the case require mention —

- 1 Sinus thrombosis with suppuration of the thrombus right up to the internal jugular termination was a very grave condition in pre-penicillin days and the treatment was attended by a very high mortality. Here a case with a metastatic lung abscess complicating the condition could be saved by a judicious use of penicillin and surgery.

- 2 Very large amounts of penicillin were required to bring about a final resolution. The total amount used after surgery was 10 million units, excluding one million units used before operation.

- 3 Some difficulty was experienced in locating the abscess after rib-resection. We resected portions of the 9th and 10th rib thinking that as the pneumonitis extended beneath the abscess cavity it would be better if we approached the abscess from the bottom. As it turned out, this led to some trouble and perhaps we would have been right on the abscess had we resected the 8th and 9th ribs.

- 4 The patient was a farmer's wife from a nearby village. Her general condition apart from the disease was very good when she was admitted and the robust constitution played a large part in her fight

against infection. Again had we an easier access to modern aids like blood, plasma, parenteral amino-acids etc., we might have been able to hasten the cure by some weeks.

My thanks are due to Dr R. N. Dixit, M.S. Chief Medical Officer, Parekh Hospital, Surat for valuable assistance and Dr D. B. Desai, M.B. B.S., Resident Medical Officer, Ashktasharam, Surat for fine team-work.

CHLOROMA

by

C. P. MUNSHI, M.D., F.C.P.S.

BOMBAY

A D., a Christian boy of 13, was admitted in the K. E. M. Hospital, Bombay, ophthalmic ward, in June 1947, for left exophthalmos and loss of vision. The proptosis of the left eye was forwards, downwards and inwards. It was non-pulsatile and irreducible. A mass, firm in consistency, could be palpated below superior orbital margin. The mass was non-lobulated and could be freely moved from superior orbital margin and the eye-ball. The upward movement of the eye-ball was restricted. The fundus examination was normal, except for a slight hyperaemia of the macular region. The general and systemic examinations were reported as showing nothing abnormal.

He left the hospital against advice but as his vision deteriorated gradually, from 6/18 to 6/36, and he developed keratitis, hypopion and panophthalmitis, he sought admission in a nearby ophthalmic hospital where his eye-ball was removed. Unfortunately, no histological examination was made of the mass removed. After the removal of the eye-ball he developed a continuous fever, for which penicillin was given, thinking it to be a septic fever, but without any result. The fever continued for a fortnight and he was transferred to the medical ward of the K. E. M. Hospital on 5-8-1947.

On admission, his temperature, pulse and respiration were 102°F, 136 per minute and 30 per minute respectively.

Physical examination showed a pale individual, with normal heart and lungs. Spleen was palpable 2 inches and Liver 5 inches below the costal margin. Lymph nodes were not palpable anywhere except a few in the groins.

Examination of the nervous system showed normal cranial nerves and upper extremities. In the lower extremities, power was lost and knee and ankle jerks were exaggerated, and ankle clonus was present. Planters were extensor on both sides. Sensations and sphincters were normal. Spine was normal.

Blood examination showed white Blood Cells 24,350 per cubic mm with 96.5 per cent lymphocytes and 3.5 per cent neutrophils. There was preponderance of large lymphocytes, suggesting immaturity and an occasional lymphoblast. Red blood cells were 1.2 million per cu mm, haemoglobin 23 per cent, and colour index 0.9. Marked anisocytosis with hypochromia was seen. No malarial parasites were detected. Triple Widal and Wen-Felix reactions were negative.

Skiagrams of the skull and spine were normal.

On 11-8-1947, six days after admission bleeding from the nose started. The nose was plugged with adrenaline pack and a blood transfusion was given, which stopped bleeding. Sternal puncture or

any other clinical investigations were refused by the patient, who was discharged from the hospital at his own request. Four days after leaving the hospital he expired.

The clinical and blood picture suggests a diagnosis of Chloroma or Chloroleukaemia. The case presents the usual three features found in cases of chloroma.

(i) A visible tumour and mechanical results of tumour formation in the orbit causing exophthalmos. The paraplegia was probably due to haemorrhage in the spinal cord, or thrombosis of the vessels, or involvement of the meninges or the cord by the malignant cells.

(ii) Toxic symptoms, weakness, fever, emaciation etc., and

(iii) Blood changes e.g. pallor, haemorrhage, and leukemia.

Chloroma is a rare, incurable disease of children and young adults, usually males. It is characterised by the presence of one or many greenish or greenish-yellow tumours, which are malignant and myeloblastic or lymphoblastic in nature, having a particular predilection for periosteum and bones of the orbit and the skull, though they are found also in the long bones, meninges and at times, throughout the viscera.

Critical Notes and Abstracts

SPOTTED FEVER TREATED WITH PARA-AMINO BENZOIC ACID WALTER J. HENDRICKS, M.D. and MICHAEL PETERS, M.D. (*Journal of Pediatrics*, January, 30 72-75). For the past few years it has been known that the chemotherapeutic agent para-aminobenzoic acid, effectively reduced the mortality from experimental murine typhus in white mice. This agent has inhibited also the growth of epidemic and murine typhus rickettsias in the developing hen's egg.

Yoemans and associates studied the therapeutic effect of this agent on human louse-borne typhus in Cairo, Egypt. Their results indicated that this disease was greatly modified, provided the drug was given early in the illness. Large doses, 24 to 28 Gm. were administered orally in 24 hours, and blood concentrations between 10 and 20 mg. were obtained. They experienced no toxic reaction other than temporary lowering of the white blood cell count in a few cases.

Rose and associates used it very effectively in one case of a white woman, aged 46, suffering with Rocky Mountain spotted fever. They administered 4 Gm. initially and then 2 Gm. in 25 cc. of chilled 5 per cent sodium bicarbonate solution every two hours. The treatment was continued for four days with blood levels ranging from 6.6 to 18.6 mg. %.

Following their suggested plan of therapy, we have successfully treated a 4-year old child infected with Rocky Mountain spotted fever. As soon as a positive diagnosis was established para-aminobenzoic acid, 4 Gm. followed by $\frac{1}{2}$ Gm. every hour with 5 cc. of 5 per cent solution of sodium bicarbonate, was given. There was no nausea. The frequency of administration was deemed necessary because of the rapid elimination of this drug. A total of 30 Gm. of para-aminobenzoic acid was administered.

Within 24 hours after the drug was started, the child became more alert and talkative, ate well without help, and sat up in bed playing with her toys. Recovery was rapid and uneventful.

Typical symptoms of rheumatic fever showed in the early days of her disease sore throat, joint pains, abdominal pain, and a heart murmur. Since some cases of rheumatic fever develop a skin rash, this finding would only add to the confusion. History of exposure to a tick was not obtained from the mother at the onset of the disease, emphasizing the extreme importance of a careful history.

EFFECT OF GLUTAMIC ACID ON MENTAL FUNCTIONING IN CHILDREN AND IN ADOLESCENTS by FREDRIC T. ZIMMERMAN, M.D., BESSIE B. BURGEMEISTER, PH.D. and TRACY J. PUTNAM, M.D. (*Archives of Neurology and Psychiatry*, November, 56, 489-506). The present experiment investigates the effect of glutamic acid on mental functioning in human subjects and is an outgrowth of a study on maze learning in the white rat. By adding glutamic acid to the diet of normal rats it was found that they learned a simple maze much faster than the control group.

A larger experiment is now in progress including children and adolescents who are mentally retarded or have convulsive disorders. The control group was selected to ascertain the effect of control of seizures for varying periods of time on intelligence.

After neurologic and laboratory examinations an initial psychometric test was performed. A dose of 6 to 24 Gm (average 12 Gm) of glutamic acid was then administered orally per day to the point where increased motor activity was apparent. This dosage was maintained or reduced, depending on the degree of motor activity evoked.

Gastric distress is occasionally observed, but can usually be obviated by discontinuing treatment for a few days and then beginning with smaller doses, which are gradually increased as tolerance develops.

The patients ranging from 16 months to 17 1/2 years were tested at the beginning and end of a 6 month period in which they received glutamic acid. Stanford-Binet, form L, Wechsler-Bellevue scale, Kuhlman-Binet, performance tests or the Merrill-Palmer test, and the Rohrschach test were used for different age levels. Retests were made after 6 months. Rohrschachs from 7 of the 9 subjects revealed increased productivity in all cases.

In the 7 patients with convulsive disorders the effect of glutamic acid raises the question whether control or reduction of seizures may result in an increase in psychologic test scores.

Several statistical studies with various drugs conclude that there appears to be no relationship between reduction in number or severity of seizures and changes of intelligence quotients.

Performance ratings were raised appreciably in a small percentage of patients in other investigations. The drug diphenylhydantoin seemed to have a greater beneficial effect in this capacity than on intelligence.

For 1 subject only was the intelligence quotient raised (1 point) whereas for 7 of the 9 patients a decrease in score occurred. The results of this study agree substantially with others reported in the literature.

The group yielded an average increase of 8 points in intelligence quotients on test, with no negative deviations. The significance of these changes becomes clearer when they are related to the age of the child.

For all subjects sharp, positive increments in mental ages are apparent after treatment with glutamic acid, low grade subjects increasing at a rate faster than in children of average intelligence

In the control group slight gain in retest performance scores is also indicated, and reduction of seizures may account for improvement on motor tests

Authors conclude that on verbal, motor and personality tests given, definite improvement following glutamic acid therapy could be observed in each of the 9 subjects during a 6-month interval Glutamic acid has a particular relation to cerebral metabolism Recent investigations suggest that release of acetylcholine is intrinsically connected with electrical changes during the nerve activity The energy of the action potential is derived from phosphate compounds An enzyme which synthesizes acetylcholine was found and this becomes in active on dialysis Addition of glutamic acid reactivates the enzyme

The precise mechanism has still to be elucidated, but it is possible to assume that the physiologic basis of the observed effects of glutamic acid is in some way related to the formation of acetylcholine

The results reported must be considered tentative because of the smallness of the group, but the consistent improvement suggests that glutamic acid may have a genuine effect on mental functioning in human subjects, as it does on maze learning in the white rat

INSULIN SUBSHOCK AS A DETOXICANT IN ACUTE ALCOHOLIC INTOXICATION by JOSEPH THIMANN, M D, and PAUL PELTASON, M D (*Quarterly Journal of Studies on Alcoholism*, March 7, 506-517) Various experiments and studies have proved that insulin by accelerating carbohydrate metabolism is always followed by a decrease of alcohol content of the blood It has been used in cases of uncomplicated acute alcoholic intoxication, Korsakoff's psychosis, delirium tremens to reduce detoxication time Daily dosage from 5 to 100 units of insulin have been administered with or without glucose Treatments were given from 3 days to 6 weeks

Authors based their technic of detoxication on these studies and employed subshock doses of insulin to 120 patients In some cases intramuscular administration of 50-60 units of insulin and intramuscular thiamin with small doses of sedatives brought a quick and uneventful recovery In some patients intravenous administration of 60 units plus thiamin and subsequent dextrose with little sedation brought an uneventful recovery Intravenous administration produced no dramatic effects Hypoglycemia started 45 minutes after injection The excellent sedative effect was even more conspicuous after dextrose was administered

The tolerance of relatively large doses of insulin should not be assumed to be universal In some cases 30 units intramuscular administration of insulin caused the patient to go into coma This was an unexpectedly strong reaction to a relatively small dose of insulin Coma occurred about 1 hour after injection The therapeutic effect, however, was good, only a minimal amount of sedation being required

An entirely different effect was observed in acute alcoholic psychosis After administration of 60 units of insulin intramuscularly patients became restless disoriented followed by semistupor and convulsions

after about 1 hour. The convulsions subsided after administration of glucose and coramin intravenously.

In these cases of acute alcoholic hallucinosis, no sedative effect resulted from 60 units of insulin. Convulsions appeared and if not precipitated by insulin they were certainly not prevented by it. A moderate amount of glucose seemed to produce the desired effect.

In cases of delirium tremens 80 units of intra-muscular insulin caused hallucinations and convulsions after 1 hour. Insulin either precipitated or did not prevent convulsions and had no sedative effect, dextrose stopped convulsions but not hallucinations, and it was necessary to resort to paraldehyde.

More satisfactory in acute alcoholic psychoses was administering of dextrose and small doses of insulin simultaneously. A full blown case of delirium tremens was eliminated within 12 hours by 3 intravenous administrations of glucose simultaneously with 20 units of intramuscular insulin twice and 15 units the third time. A minimal amount of sedation was used.

120 patients were studied, 18 had acute alcoholic psychoses, aging from 24-69 years. Duration of bouts ranged from 1 day to 8 months while duration of drinking varied from 6 months to 27 years. The smallest consumption was 1 pint, the highest 8 to 4 qts daily. Determinations of alcohol in the blood revealed concentrations between 150-480 mg per 100 c c.

Coma developed in 28 patients in the course of treatment, in 28 instances the sobering-up process required a single repetition of insulin. The smallest dose of insulin was 10 units, the largest 80 units.

In the alcoholic psychoses 10 to 20 units of insulin given simultaneously with dextrose proved the method of choice. Uncomplicated acute alcoholic intoxication responded best to subshock doses of insulin. Minimal amounts of sedatives were administered and in most cases omitted entirely.

The duration of the sobering up process was reduced to 1 day, and often to only a few hours.

The technic is not limited by age.

Patients prefer this to the conventional method of substituting paraldehyde or chloral for alcohol.

In 80 per cent of these cases the insulin technic proved to be definitely superior.

TREATMENT OF MUSCULAR CRAMPS WITH VITAMIN B₂ The value of vitamin B₂ in the treatment of muscular cramps is discussed by L. Roughes (*Presse Med. calc.*, June 28, 1947, 55, 441), who cites the results obtained and reported by Perrault, Bouvier and Boulanger (*Paris Medical*, 1946, 36, 549). Following the treatment of a forty-eight year old man with chronic oxycarbonate poisoning manifested almost exclusively by painful muscular asthenia, who was given vitamin B₂ in dosage of 18 mgm daily by mouth, and who showed remarkable improvement after the second day's the authors treated a number of patients with muscular cramp of varied origin—diabetes, circulatory disturbances, infections, and diverse cases of intoxication,

with equally good results. The usual dosage was 15 to 25 mgm daily, but higher dosage can be employed without fear of toxic reactions.

CARROTS GIVE LONGER LIFE (*Science News Letter*, April 19, 51 248, 1947) "Get on the carrot wagon if you want to add extra 10 years to your life at its prime."

This advice seems justified on the basis of latest nutrition studies by Dr. Henry C. Sherman of Columbia University. Rats given four times the normal amount of vitamin A in their diet lived more than 10 per cent longer than their life expectancy. And carrots are a very rich food source of vitamin A for humans.

The increased length of life comes at the prime of life in the rats and would in humans, too, Dr. Sherman thinks. The rats with the extra vitamin A grow more rapidly and more uniformly and have more vigorous offspring.

Vitality is higher and death rates lower at all ages. Full adult capacity, or the prime of life, is reached earlier and kept longer. Life expectation is increased not only for the young but also for grown-ups.

"The previous general progress of public health had increased the life expectation of the infant but not of the grown person," Dr. Sherman points out. "Now the nutritional improvement of the norm raises the life expectation of the adult as well."

"The extra years thus offered are not to be pictured as added to old age. Rather it appears that something like an extra decade can be inserted at the prime or apex of the life lived in accordance with today's newer knowledge of nutrition. Life becomes longer because it is lived on a higher health level throughout. The apex of attainment is higher, the period of prime is longer and, in human terms, there is a smaller percentage of years of dependence."

TREATMENT OF ACUTE NEPHRITIS BY ANTI-HISTAMINE SUBSTANCES—Whilst there is still no unanimity as to the etiology of acute glomerulonephritis, the general consensus of opinion at the moment is that it is an allergic reaction—usually to a haemolytic streptococcal infection in the upper respiratory tract. Starting from this hypothesis, Francis Reubi (*"Le traitement de la nephrite aigue par les antihistaminiques de synthese"* Basle Benno Schwabe & Co 1946) has investigated the action of antistine, one of the recently introduced synthetic antihistamine drugs. The preliminary experiments on rabbits indicated that antistine was of value both as a prophylactic, when given early enough, in preventing the onset of acute glomerulonephritis, and in apparently curing it when given within a reasonable time of the onset of the condition. The clinical material consists of only seven cases of glomerulonephritis, but the results are described as "more than encouraging." Full records are given of these patients. No beneficial effects were noted in chronic nephritis. The usual dosage of antistine was 0.1 to 0.2 gm. every three hours for the first week, some being given by mouth and some intramuscularly. Subsequently the dosage was gradually reduced. The total period over which antistine was given was up to three weeks. Stress is laid upon the necessity for giving the patient a low-salt, low-protein diet with ample vitamins.

THE TREATMENT OF MOTION SICKNESS—A report of the results of an investigation carried out under the auspices of the

National Research Council of Canada for the evaluation of drugs for the prevention or alleviation of motion sickness is given by R L Noble, E A Sellars, and C H Best (*The Canadian Medical Association Journal*, April, 1947, 56, 417) Of the belladonna alkaloids hyoscine is the most effective, but a mixture of hyoscine and hyoscyamine may have less unpleasant or dangerous side-effects It was found in healthy young men of average size (70 kgm) that an initial dose of 0.3 mgm hyoscine HBr plus 0.8 mgm hyoscyamine HBr was effective, protection lasting from six to ten hours Subsequent doses should not exceed one-half the initial dose and should be separated by an interval of eight hours or more The only adverse effect noted was dryness of the mouth Children have a lower tolerance to belladonna than adults Of the barbiturates, V-12 (ethyl-B-methyl-allyl thiobarbituric acid Abbot Laboratories), whilst having as good or better protective properties, has such a low depressant action that doses of 315 mgm or more could be tolerated without undesirable side-effects There is considerable individual variation to effective dosage, but it was found that the best results were obtained when therapy was instituted on the day before exposure to motion Divided doses are preferable and few individuals show undesirable reactions if 155 mgm is taken with breakfast and 155 mgm with supper Taking V-12 with meals is desirable as absorption is prolonged thereby In resistant cases an extra 155 mgm may be taken with the midday meal Therapy should be continued during short trips, but the duration of protection after the drug is stopped is about fifteen to eighteen hours The immediate symptom of overdosage is sleepiness, which should be used in assessing individual tolerance, and is a contraindication to increase of dosage It is stated that in no case should a total daily dosage of more than 460 mg be used, and in cases requiring this large dosage a reduction after one or two days is advisable A mixture called the "Canadian Motion Sickness Remedy" and consisting of

Hyoscine HBr	0.1 mgm.
Hyoscyamine HBr	0.8 mgm
V 12 (ethyl B methyl allyl thio barbituric acid)	180.0 mgm.

is commended, the suggested dosage being 2 capsules taken two to four hours before exposure to motion, followed by one capsule every eight to twelve hours In highly susceptible individuals the therapy may be started twenty-four hours before exposure to motion Dosage should be reduced on the occurrence of undue hypnosis and dryness of the mouth, and in no case should more than three capsules be taken in twenty-four hours For children and small adults the dosage should be reduced Treatment with these capsules should never be given for more than five days each week or undue accumulation of the thiobarbiturate may occur

Our Problems : a forum for discussion

AYURVEDIC AND UNANI SYSTEMS

THEIR POSITION IN MODERN MEDICINE

In considering the questionnaire sent by the Government of Bombay about the steps to be taken to improve the teaching of Ayurvedic and Unani Systems of Medical Treatment, one might well remember the fact that the East India Company was successful in India because of its having some Surgeons trained in Western System of Medicine. One of them cured the Emperor's daughter in Delhi of a simple malady which the Unani Physicians at Court found difficult to diagnose or cure. The knowledge possessed at the period in these systems of medicine must have been of a very high standard. European medicine has advanced considerably since that time, while Unani and Ayurvedic systems of medicine have remained stagnant. As regards their theory about the structure and function of the different organs and tissues in the body, the less said the better, in comparison with present sciences of Anatomy and Physiology. Ayurvedic Medicine at present is nothing more than prescribing of concoctions made from Indian drugs prescribed empirically on symptoms of certain humors observed in ancient times without knowing their etiology whether bacterial, parasitic, or metabolic. For diagnosis of diseases, no chemical examination of urine or blood is known, chest diseases are diagnosed without stethoscope. Feeling of pulse of the right hand in males and left hand in women are the only methods for diagnosis of diseases and knowledge of midwifery and gynaecology is non-existent or rudimentary.

We cannot but regret that the practice of Ayurvedic medicine is mixed up partly with astrological arrangement of planets at the time of the illness and sometimes with deities presiding over certain diseases. The Ayurvedic or Unani physician in the old times was for the use of kings and emperors with no conception of his being of any use for the community at large whether in villages, towns, cities or armies. This has never changed as has been noticed from the records in the diaries of the various Viceroy and Governor-Generals. The East India Company never had any difficulty in enlistment of soldiers for their various armies, most of the men coming from sepoys in the pay of the Indian rulers, the main reasons being, the care they received as regards hygienic environment of their quarters, the care for the food and water and the after-care they received when wounded in the battle-field, besides the regularity with which they received their salaries.

The rapid progress of science, technology and industry has brought about social changes. Life is getting more complex. There has been specialisation in medicine as well in other fields. We have great doubts that the Ayurvedic and the Unani systems with their goal of treatment of a person who is ill has anything in their systems as regards prevention of illnesses in communities.

The present push for Ayurvedic and the Unani systems does not come from the man in the street, but from some highly placed individuals who might have been cured of their disease by these systems, where European drugs had supposedly failed, and from the manufacturers of Indian herbatic and other drugs, the owners of pharmacies and rasashalas who have vested interests in the sale of their products. The use of these Ayurvedic and Unani drugs is called by them

systems of medicine Western system of medicine does not preclude any of these Unani or Ayurvedic drugs

Ayurvedic medicines might be of use even in the present time where individual and community life and relationship with one another has not changed, but such places are not many. Even in the times of early Mogul Emperors when Ayurvedic and Unani systems were at the height of their development, the physicians from the West were consulted for the treatment of the Royal relations and received rewards in the way of freedom for trade and commerce for Western people in this country. The Royal family of Nepal solely under the Ayurvedic medicine became practically extinct in the year 1816 due to the death roll of all its members except a child of two years, the King having postponed his own vaccination for an auspicious day during an epidemic of small pox in 1815, though advised by the British Resident for getting vaccinated as quickly as possible (*vide Private Journal of Marquis of Hastings*). The new conditions of the last war produced new emergencies as regards injuries to human bodies. Scientific advances and new discoveries in drugs, new surgical procedures and emergency measures have changed Western medical outlook even within the last few years. As regards causes and treatment of various diseases new diseases have been diagnosed whose presence was not noticed in the last century. That Ayurvedic medicine could not have had slightest chance for successful treatment of diseases and injuries of the present war where poisonous gases and bombs of exceptionally high explosive power were used would be accepted by all reasonable people. The proper position of mosquitoes, bugs, and flies as regards their etiological factors for malaria, dysentery, typhus, dengue, elephantiasis has never been stated in those systems of medicines. Immunisation by vaccination in plague, tetanus, typhoid, dysentery and small-pox has no place in these systems. Nobody can say that the treatment by vaccination is not as efficacious as Ayurvedic or Unani drugs and most of the people practising as Ayurvedic Vaidyas or Unani Hakims have adopted the treatment by these measures, sometimes with unforeseen results on account of want of knowledge in the use of these remedies.

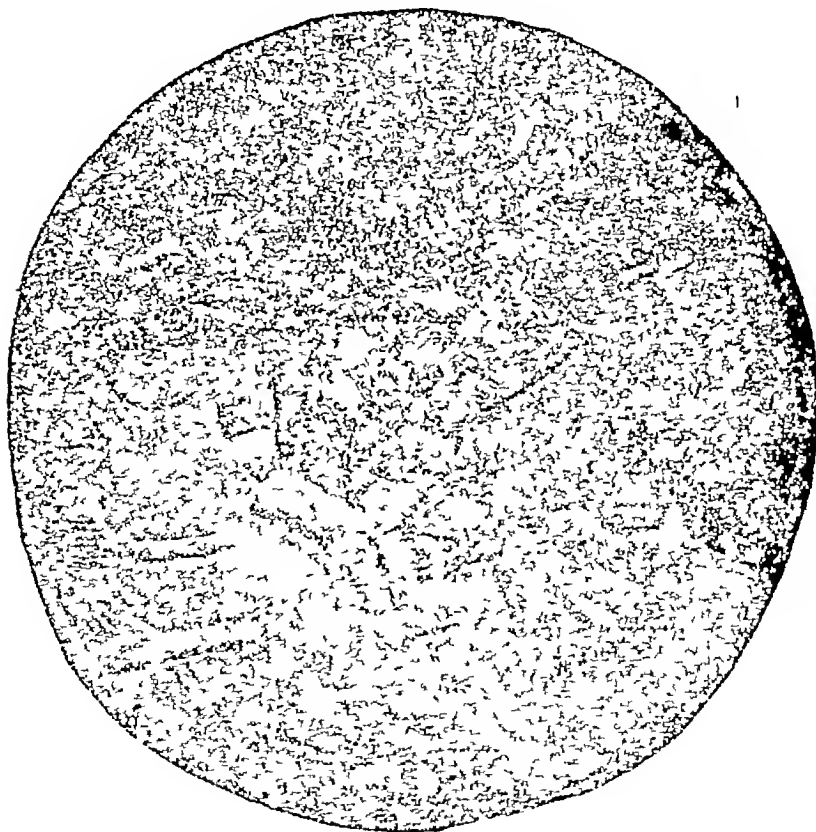
The new discoveries in Chemotherapy and Immunity for malaria, typhoid, dysentery and plague in communities where Western systems are followed, which have resulted in an increase in the expectancy of life, apart from freedom from morbidity, should convince any Government of the futility of reviving these old systems for basic training of individuals for practising by methods even in these so called systems. There may be some drugs which may be cheaper and more effective in these systems. The investigation of these is alone needed, and money may be spent rationally for this purpose through the existing channels. The basic training of a medical man, whether on Ayurvedic or Western Systems should be the same. The proposal of the Government to establish colleges for the teaching of Ayurvedic or Unani systems though vigorously propagated by politicians and some rich merchants having no knowledge of what these systems are, is met with considerable disfavour and apprehension by almost the whole of the medical profession. The man in the street who receives treatment has no voice in this propaganda. The present medical man is ready to accept any drugs or methods of Ayurvedic, Unani, or Homoeopathic system provided they are useful.

We think an intensive research is all that is needed by the present Government at the present time, about the usefulness of Indian drugs and the different ingredients in their composition and all schools for these systems must be abolished in the interests of the country, otherwise it will take a number of years to undo the harm done to the people by the unthinking patriotism of a few well-meaning but ignorant enthusiasts to revive the dead past, which alas ! is unrevivable

S B GADGIL, F.R.C.S

Pres dent

BOMBAY MEDICAL UNION



HUMOROUS SCENE ON A CIRCULAR MEDALLION A BUDDHIST MONUMENT, THE STUPA OF BHARHUT 3rd CENTURY B C (Alexander CUNNINGHAM, *The Stupa of Bharhut* London, 1879)

THE EARLIEST DENTAL CARICATURE

"A caricature is a representation of distinguishing characteristics of man or things in a form purposely exaggerated to the point of grotesquery so that the whole, in spite of its resemblance to the original, looks ridiculous

"Even the earliest representation so far found caricaturing a tooth extraction fills this definition Here we have a gigantic forceps

Reflections and Aphorisms

"The phases of a doctor's life are often three. The story of Vesalius shows it well. There was that *first* fierce stage of youthful curiosity and research when a restless mind challenged, with courage, the teachings of Galen which had become almost a dogma of the Church. This was the fertile season of his mind. Who will know the motive which finally drove him to destroy so many writings? But, soon we find him in the *second* stage after the enjoyment of so great achievement, and after bitter criticism he is at ease in a courtly life, all effort at research slackened. It is a base period of private satisfaction and public adulation, the mind stagnant in official ostentations. Was it misfortune or the ripening through experience which again quickened the sleeping spirit and made him see the paltry character of his part, or was it revulsion from the empty social rounds, that sent him, penitent, a man not yet old, towards the Holy Land? But now he has reached the philosopher's phase, *the last*, when the worthlessness of things ephemeral appals him and under the strong light of an ancient faith he sees himself magnified to no more than a man's littleness. Then on the voyage home death, sudden and unheralded, casts him unrecognised on a lonely shore.

On humbler planes many of us have shared similar vicissitudes. We have our earnest serious years of unselfish enquiry when the pursuit of knowledge seems all and when at times we grow priggish with our knowing. Follow the urbane years of our self-satisfied success. We are kinder and more patronising now. This is the happy interval of the mind's stasis. We seek to hide the ravages of time in the puerilities of golf and bridge, children, again seeking diversion with our childish toys. Tragedy or loss or some fortuitous word cuts through these weeds and shows the deeper roots. Whither go they? Suddenly we see technique is not all! Life is more than pulsing blood in an artery, happiness far other than a tickling of the senses. Lucky is he who having his journey to the Holy Land completed, finds, in a sanctified mood, ease for the crossing.

For me the days of active sport were soon over. They had their value hardening the body, or encouraging the timid spirit of ostentatious boldness. It was the external life—a life of little chivalries without. The curiosities of the mind lasted unsatisfied till I was over fifty, the hunger of the senses not to so long. But even in the satisfaction of a fleeting suburban success, the spectre of evanescence was now always stalking me. I distrusted all the little baubles even while I treasured them. In these last moments their values are seen in their true inflation. Yet even now I finger this worthless currency, loth to let them go."

HERBERT MORAN—IN MY FASHION, (1946, SYDNEY, DYMCK'S)

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